MAY 1951

BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

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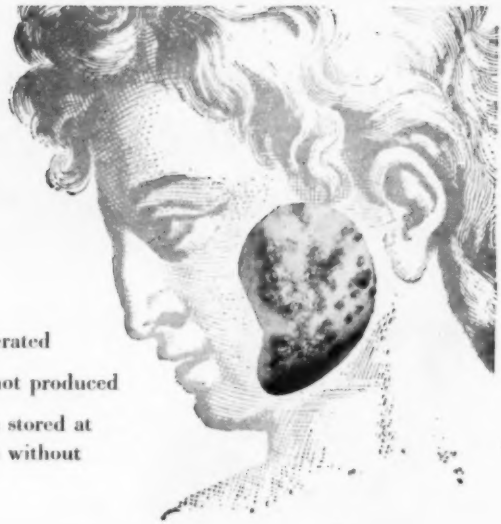

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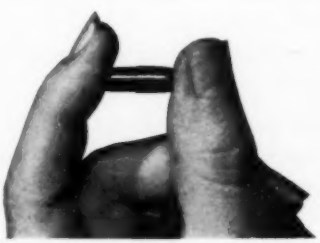

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MAHLON ASHFORD, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
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VOL. 27, NO. 5 MAY 1951

PRIMARY CANCER OF THE LUNG WITH SPECIAL CONSIDERATION OF ITS ETIOLOGY*

EVARTS AMBROSE GRAHAM

Bixby Professor of Surgery, Washington University School of Medicine, St. Louis, Missouri

I APPRECIATE very much the high honor which you have accorded me in inviting me to give this fifth James Ewing Memorial Lecture. Many years ago when Dr. Ewing first published his "Neoplastic Diseases" I was greatly stimulated by it. I wish sincerely that he was still alive to help solve some of the pathological problems concerned with the subject about which I am going to speak to you tonight.

Bronchiogenic carcinoma differs from other cancers in two important respects, 1) it has shown an enormous increase in the last thirty-five years and 2) there has been a progressively larger incidence in the male sex.

There can no longer be any reasonable doubt that the very great increase in the incidence of bronchiogenic carcinoma is real and not merely apparent. Kennaway and Kennaway,[1] in a study of death certi-

* The Fifth James Ewing Memorial Lecture delivered at The New York Academy of Medicine, May 4, 1950.
From the Department of Surgery, Washington University Medical School and the Barnes Hospital, St. Louis.

ficates in England and Wales, found evidence of a great increase from 1928 to 1945, and more recently Doll and Hill[2] quote a British government report which shows that for the twenty-five year period from 1922 to 1947 the incidence of the condition found in autopsies in England and Wales increased fifteen times over what it had been previously. Actual figures on the increased incidence in the United States during the same period are not available but it is noteworthy that although Adler[3] in 1912 could collect only 374 cases from the world's literature, individual experiences in this country greatly exceed that total of reported cases from the whole world. For example, at the Barnes Hospital we have had 1375 proven cases in the last thirty years, or nearly four times as many as Adler could collect from the world's literature. In the United States statistical studies at the Charity Hospital of New Orleans by Ochsner and DeBakey,[4] at the St. Louis City Hospital by Wheeler[5] and at the Hines Veterans Hospital by Ariel, Avery, et al.[6] have all shown that in recent years bronchiogenic carcinoma has become the most frequent visceral cancer of the male patient. Cancer of the stomach which formerly occupied first place has been relegated, at least in those institutions, to second place.

No one can deny that there were excellent pathologists in the last century who certainly knew cancer when they saw it. It seems hardly likely that those of the caliber of Virchow, Cohnheim and Rokitansky could have missed recognizing the condition at autopsy as frequently as would have been necessary to account for the pronounced difference in incidence then as compared with now. Moreover, the argument advanced by some that the increase is only apparent because more people are reaching the cancer age now loses value when one realizes that not only is the number of cases increasing but, more striking, this cancer has changed its relative position in frequency. The fact that more people are now reaching the cancer age would not explain how it has happened that bronchiogenic carcinoma has advanced to a position of first place in men from one of about eighth place in frequency—and this all within the last thirty-five or forty years.

Along with the increased incidence of the condition there has also been a progressive distribution in favor of the male sex. For example, when Adler compiled his statistics the ratio of males to females was about three to one. In contrast, in our last 150 cases the ratio was 18.5 males to one female. In 100 consecutive cases collected by Lindskog[7]

between 1938 and 1943 he found the ratio 4.5 to 1 but in another series in 1947 and 1948 it had become twenty-four to one.

The preponderance of incidence in males raises the question of whether sexual factors play a role in conferring a relative immunity upon the female sex. In other words, does the state of femininity make it less possible to develop a bronchiogenic carcinoma?

To gain information on this question Kemler and the writer[8] used Greene's[9] method of transplantation of small fragments of human bronchiogenic carcinoma from a male subject into the anterior chamber of guinea pigs' eyes. Our experiments showed that the transplantation was equally successful in both female and male animals. Likewise Gumbreck[10] in assaying the male sex hormones in ten cases of bronchiogenic carcinoma in men found that there was no essential difference between the cancer subjects and normal controls of the same ages. Therefore it seems that the state of masculinity or femininity has no inherent quality that is responsible for the marked preponderance of incidence of bronchiogenic carcinoma in men.

From all of this it seems reasonable to assume that there has been something in our culture or methods of living in the last thirty or forty years which has been responsible for the remarkable increase of this cancer and that men have been more exposed to this carcinogenic influence than women. Occupational factors would seem to be relatively unimportant since all economic classes and men engaged in all kinds of occupations seem to be affected. The butcher, the baker and candlestick maker all are prone to have the condition. Moreover both urban and rural dwellers seem to be subject to it about equally.

When one speculates on what factors we are exposed to now different from those in existence formerly, various possibilities suggest themselves. One of these of course is the great increase in the use of petroleum products since this is the automobile age. Preliminary observations on this point, however, fail to show that oil field workers, garage mechanics and others particularly exposed to petroleum products or to inhalation of exhaust fumes from automobiles have a significantly greater incidence of the disease than others. Without mentioning other possibilities for which there is no striking incriminating evidence at the present time we can take up for consideration immediately one factor which seems to be very important. That factor is tobacco smoking, especially the use of cigarettes.

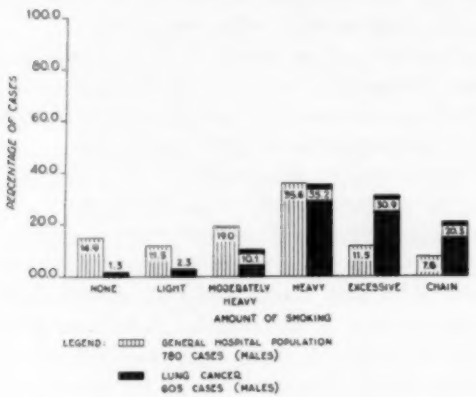

Fig. 1—In this chart a comparison is made between the amount of smoking done by 605 male patients with bronchiogenic carcinoma and 780 men without lung cancer of approximately the same age groups, economic status and percentage of urban and rural residence. "Light" smokers have used from 1 to 9 cigarettes per day for more than 20 years. "Moderately heavy" indicates 10 to 15 cigarettes per day for more than 20 years. "Heavy" smokers are those who have used from 16 to 20 cigarettes per day for more than 20 years. By "excessive" is indicated the use of from 21 to 34 cigarettes per day for 20 years, and by "chain" smokers is meant those who have used 35 cigarettes or more per day for at least 20 years

The idea that smoking may be an important factor in the etiology of bronchiogenic carcinoma has been suggested by many writers. Adler made such a suggestion in his monogragh. Tylecote,[11] Hoffman,[12] McNally,[13] Lickint,[14] Arkin and Wagner,[15] Roffo[16] and Müller[17] were additional workers who prior to 1940 thought that smoking, especially of cigarettes, was important in this respect. In 1941 Ochsner and DeBakey[18] called attention to the similarity of the curve of increased sales of cigarettes in this country to the greater prevalence of primary cancer of the lung.

Recently Wynder and the writer[19] made the largest statistical study of this question reported up to that time. A survey of the smoking habits was made in 684 proven cases of bronchiogenic carcinoma. The information was obtained by means of a personal interview with each patient.

A standard questionnaire was used and most of the interviews were made by two non-medical women who were ignorant of the diagnosis at the time they questioned the patients. The subjects of the interviews were from all social and economic classes and from widely scattered parts of the country. It was found that of 605 males with bronchiogenic carcinoma, other than adenocarcinoma, 96.5 per cent had smoked more than a half pack of cigarettes daily for more than twenty years as compared with 73.7 per cent of 780 males without lung cancer who had smoked as much and who were of a comparable age group. Even more impressive was the fact that among the lung cancer group 51.2 per cent had smoked more than a pack a day for at least twenty years as compared with only 19.1 per cent who had smoked that much in the group without lung cancer. In only 2 per cent of these cases did the patient not smoke at all or less than one-half pack of cigarettes daily. The most striking features revealed from the study were that in the correlation which seems to exist between cigarette smoking and bronchiogenic carcinoma apparently it is necessary that the man be a heavy smoker (at least a half pack of cigarettes per day) and that he has smoked for a long period of time (usually twenty years or more). (Fig. 1).

The commonly held belief that women smoke as much as men and that therefore they should show as great an incidence of bronchiogenic carcinoma as men is not borne out by a statistical study. In order to investigate this point two groups of hospital patients without lung cancer were interviewed. All of them were more than thirty years of age and they were comparable as regards economic status. One of these groups consisted of 552 women and the other of 780 men. Of the women it was found that 79.6 per cent were nonsmokers and only 1.2 per cent had smoked more than a pack of cigarettes a day for at least twenty years. By contrast this percentage of 1.2 is to be compared with one of 19.1 found in the males who did not have lung cancer. It is an interesting coincidence that this ratio of 19.1 to 1.2 compares closely with the sex ratio of incidence of bronchiogenic carcinoma, which was 18 males to 1 female in our last 150 cases. It is chiefly the girls and young women who are the female heavy smokers and they have not yet had time to smoke for twenty years or more. Perhaps in another decade or so there will appear a marked increase in the incidence of bronchiogenic carcinoma in the female. At present, and presumably during the time that the disease has been showing its great increase, it seems clear that men have been

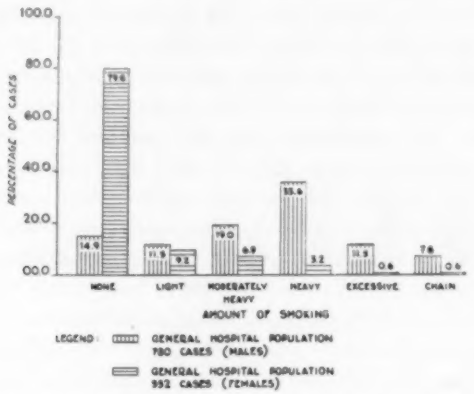

Fig. 2—Chart which shows the error in the belief that women in the cancer age (more than 40 years old) have smoked as much for as long (20 years) as men of the same age group. The designations "light", "moderately heavy", "heavy", "excessive" and "chain" have the same meanings as in Fig. 1.

much more exposed to the consequences of smoking than have women. Thus the greater preponderance of lung cancer in men may perhaps be explained (Fig. 2).

Of importance in considering a possible relationship between cigarette smoking and bronchiogenic carcinoma is the interesting article of Dungal,[20] the Professor of Pathology at the University of Iceland. He finds that in that country primary cancer of the lung is still a comparatively rare disease, being ninth in frequency among carcinomas of various organs. At the same time the amount of cigarette smoking is very much less than in other countries. For example, in 1932 the per capita consumption of cigarettes in Iceland was only one-eighth of that in the United Kingdom. Since World War II, however, the amount of cigarette smoking has greatly increased, but presumably an insufficient period of time has elapsed to have an effect on the incidence of bronchiogenic carcinoma.

The evidence, therefore, seems at least suggestive that excessive cigarette smoking carried out for a long period of time (twenty years or more) has been a factor in causing the remarkably increased frequency

of bronchiogenic carcinoma during the last thirty-five years. The proof is lacking and will remain absent until it becomes possible to produce cancer experimentally from some or all of the products contained in cigarette smoke. Various possibilities as to the source and nature of the carcinogenic substances come to mind. Of importance could be tars contained in the smoke and inhaled into the lungs, substances contained in the paper, such as arsensic, insecticides used in the growth of the tobacco, etc.

Another point brought out by the study of Wynder and the writer[19] is that if a man was an excessive smoker a few years ago the fact that he may have stopped smoking recently does not preclude the possibility that the smoking may still have been an important factor in the development of his recently acquired bronchiogenic carcinoma. This phenomenon is analogous to the lag which is well known to occur experimentally in the mouse between the application of a carcinogenic agent and the appearance of the tumor.

Of course, it is realized that excessive cigarette smoking is not the only etiological factor. After all in 2 per cent of our cases the patients had never smoked. Similarly it is well known that not every man who has been even a chain smoker for many years develops a primary cancer of a bronchus. There are no data available at present to indicate just what risk of developing such a cancer a man takes when he indulges in excessive smoking over a long period of time.

The common variety of bronchiogenic carcinoma, and the one which has shown the remarkable increase, is the epidermoid or squamous type. In many others the pathological diagnosis is "undifferentiated" type. Many histological varieties have been described by different pathologists. The most common designated types, other than those just mentioned, are the adenocarcinoma, the round cell and the oat cell carcinoma. There is considerable doubt, however, about the correctness of assuming that these so-called morphological differences noted in cell arrangements and types really represent different varieties of cancer. In many cases an examination of different parts of the same tumor will reveal morphological variations which could easily lead to different diagnoses if one should adhere too closely to rigid classifications. For example, if one recognizes a round cell or an oat cell carcinoma as a distinct type from an adenocarcinoma he may have difficulty in supporting his case if he will examine other parts of the same tumor. In general,

however, it seems to the writer that perhaps two common types occur, of which one is the epidermoid or squamous variety and the other the adenocarcinoma. Most of those tumors which are designated as undifferentiated seem to be less differentiated variants of the epidermoid type.

The importance of considering the morphological varieties here is that perhaps one can think of the epidermoid carcinoma of the bronchus as being a fundamentally different disease from the adenocarcinoma, at least in so far as its etiology and pathogenesis are concerned. At any rate that is a concept which the writer would like to suggest with the full realization of the danger of placing too much reliance on morphological classification. To some pathologists it may seem an error even to recognize the existence of adenocarcinoma of the bronchus. Yet unquestionably there are bronchial carcinomas which present microscopically an adenoid arrangement of the cells suggestive of an attempt to form glands. In our experience one finds such tumors about equally distributed between the two sexes and they are far less common than the epidermoid or squamous variety which is the ordinary tumor occurring predominantly in males.

According to the suggested concept one can think of the epidermoid or squamous carcinoma as being caused by a transmutation or metaplasia of adult bronchial epithelium due to the action of carcinogenic influences of which cigarette smoking seems to be an important one. On the other hand there is some evidence that the group of tumors, commonly called by various names such as bronchial adenoma, cylindroma, carcinoid, oat cell, round cell or adenocarcinoma in many instances may arise from fetal bronchial buds which have remained dormant until adult life. The evidence for this idea will be presented later. Here, however, it may be stated that if this concept is true those tumors just mentioned, which are either potentially or actually malignant, may be thought of as a conversion of embryonic epithelium rather than adult epithelium into cancer cells. This group of cancers then should be regarded as representing an entirely different condition from the ordinary common variety of epidermoid or squamous bronchiogenic carcinoma.

Fried[21] in 1934 proposed that the bronchial adenoma originates in the bronchial mucous glands. Previously Reisner[22] in 1928 and Wessler and Rabin[23] in 1932 had postulated more specifically that the origin was the epithelium of the ducts of the mucous glands. In 1941 Goldman and Stephens[24] considered that the tumor can come from the epithelium of

either the ducts or the glands. Stout[25] likewise in 1943 considered the bronchial glands to be the origin. In 1950, in an excellent review of the subject of adenomatous tumors of the bronchi, Goldman and Conner[26] propose that the epithelial cells of the serous and mucous glands of the trachea and bronchi, or the ducts of these glands, form the origin of the so-called bronchial adenomas, the cylindromas, the carcinoids, the so-called mixed tumors and the carcinomas which may arise from any of them. There is no good reason to doubt the correctness of any of these hypotheses. None of them really is opposed to the idea advanced by Womack and the writer[27] in 1938, that the so-called bronchial adenoma is derived from a fetal bronchial bud which has remained dormant. The only disagreement that can be said to exist is that according to our theory many of the varieties of tumor just mentioned arise in latent embryonic bronchial buds which contain the bronchial glands, whereas the authors just quoted apparently assume that the tumors arise from adult and fully formed glands and ducts. Harris,[28] after a study of human fetuses and newly borns, points out the similarity of infantile types of structures, especially the bronchial mucous glands and the peribronchial and peritracheal lymphadenoid tissue, to the histologic findings in bronchial adenoma. Since, in the material studied, the bronchial mucous glands occurred not only just beneath the mucosa but more deeply between the cartilaginous rings, and since the lymphadenoid tissue was found not only peribronchially and peritracheally but within the walls of bronchi and trachea as well, Harris states that it can be deduced that tumors arising from such tissues may be intramural or extramural or may extend into the bronchial or tracheal lumen. He also mentions the well-known fact that adenomatous tumors have been found in childhood and refers to the article by himself and Schattenberg[29] in which several such tumors in children, one only seven days old, were reported. Finally he states that his observations are compatible with the observations and ideas of Womack and the writer.[27]

One reason for regarding the group of tumors commonly designated as adenocarcinoma, as well as oat cell, round cell carcinoma, cylindroma and carcinoid as essentially a different condition from the epidermoid or squamous cancer of the bronchus is the fact that there is no convincing evidence that cigarette smoking has any etiological influence in the production of the former group of cancers. In fact when a bronchiogenic carcinoma occurs in a patient, male or female, who has never been a

smoker it is more likely to be one which is diagnosed as an adenocarcinoma or one of its variants (oat cell, round cell carcinoma, etc.) than as an epidermoid carcinoma. Moreover there is no evidence that the adenocarcinoma has participated in the striking increase in bronchiogenic carcinoma in general. Although apparently there are actually more cases of adenocarcinoma found than formerly, the small increase in this type, in contradistinction to the large number of cases of epidermoid carcinoma, can probably be accounted for by such factors as the greater number of people in the cancer age nowadays, better means of recognition, etc.

According to the concept mentioned above it seems tempting to assume that those carcinomas designated as adenocarcinoma, oat cell and round cell carcinoma arise from an embryonic bronchial bud which has failed to develop into normal tissue and has remained dormant for many years before being transformed into a carcinoma. The fact is of course well established that in the growth of the embryo the lungs are formed by a process of budding from the trachea which in turn is formed from the embryonic foregut.

In developing this concept the so-called bronchial adenoma furnished the first suggestion. Often the microscopic appearance of this tumor resembles fetal lung so closely that it is practically impossible to distinguish it from the lung of, for example, a 16 weeks old human embryo. So far as I know the first one to note this similarity was Bremer[30] of the Department of Anatomy at Harvard who reported it to Churchill.[31] For the most part the cells contain very little cytoplasm so that they give the appearance of consisting chiefly of nuclei. Moreover they are usually round or oat shaped.

The next point to establish was whether or not these so-called adenomas ever become malignant by developing into carcinomas. When in 1938 Womack and I[27] offered evidence that this tumor is potentially malignant as demonstrated by the invasion of neighboring lymph glands, we found no supporters of the idea. For example, in 1941 Foster-Carter[32] of the Brompton Hospital, London, from a study of twenty-two cases, stated that he had found no evidence of malignancy except perhaps slight invasion of the bronchial wall in a few instances. Strangely also in 1944 Engelbreth-Holm[33] of the University Institute of Pathological Anatomy of Copenhagen in an article which carried the title of "Benign Bronchial Adenomas" concluded that there was little evidence that those tumors

ever become malignant although in all of his twelve cases he reported there was marked invasive growth. Now, however, many cases of undoubted malignancy have been reported in which metastases were found at autopsy not only in the regional lymph glands but in the liver and other distant organs as well. (See, for example, Adams, Steiner and Bloch,[34] Anderson,[35] Stowell,[36] Bigger,[37] Alexander[38] and Chamberlain and Gordon[39].) In 1945 Womack and I,[40] in a paper presented to the American Association for Thoracic Surgery, reported two cases in which autopsy was performed after bronchoscopic biopsies had established the diagnosis of so-called adenoma. In both cases metastases were found in the liver. In one case the bronchoscopic biopsy had been made four years prior to the death of the patient. In the carcinomas which arise in the so-called adenomas the cellular structure corresponds closely with that of the latter tumors. In other words the prevailing type of cell is one which has very little cytoplasm and therefore seems to consist chiefly of nucleus. It has the morphological characteristics of the oat cell or round cell seen in those carcinomas which are designated by some pathologists by those names. Often also the cells are arranged in groups which are strongly suggestive of an adenoid structure and because of that arrangement many pathologists would use for the tumor the name of adenocarcinoma.

Criticism against the concept that the so-called adenoma and the carcinoma which is derived from it may represent an embryonic bronchial bud which has remained dormant without forming normal lung tissue has been made on the ground that if this conception is correct then one should expect often to find such buds during the routine examination of lungs. It should be understood, however, that they are of microscopic size unless they have become enlarged sufficiently to be recognized as tumors.

In 1904 Albrecht[41] coined the term "hamartoma" for a peculiar tumor of the liver. By this term he meant to imply that it was an expression of an abnormal growth of the normal structures of the organ. The word is derived from the Greek word, "hamartia," which means failure to reach the goal. The idea of Womack and the writer that some of the tumors of the bronchi and lungs result from the failure of embryonic bronchial buds to develop into normal adult structures is in line with Albrecht's conception of "hamartoma" concerning his tumor of the liver, and in our article of 1938[27] we called attention to the similarity

of our own conception of the origin of these tumors to that of Albrecht for the tumor of the liver described by him. Probably also of a similar nature are the carcinomas which we[42] reported arising in congenital cystic disease of the lung and in association with other developmental abnormalities of the lung. Although some of the recent writers have applied the term "hamartoma" to the tumors which seem to us to arise in fetal bronchial buds, most authors still designate them as bronchial adenomas. Perhaps it is fair enough to state that even the use of the term hamartoma implies that the tumor has arisen in an embryonic rest. Those who use that term therefore seem unconsciously to agree with our conception of its origin.

In our first article in 1938 Womack and I[27] noted a resemblance of these tumors to the mixed tumors of the salivary glands and therefore proposed the name of mixed tumors of the bronchus. The reason for this suggestion was that in some of the cases we found cartilage and even bone, and in some there was an adenoid arrangement of the epithelium like that often seen in the salivary gland tumors. Names, however, are of little importance.

Of passing interest is the possibility that some of the tumors of the bronchus, other than those of predominantly epithelial type, also may arise from embryonic buds. For example, a chondroma, a fibroma or a lipoma may have such an origin. The embryonic bud is composed not only of endoderm but of course of mesoderm as well. The latter is destined to form connective tissue, smooth muscle, bronchial cartilage, and any other tissue of mesoblastic origin. If, therefore, the mesoblastic tissue reacts abnormally to some unknown growth stimulus a tumor may arise in which mesoblastic tissue will predominate. The chondroma, fibroma and lipoma could perhaps be explained on that basis. Although those tumors are rare we have had several examples of each kind. Possibly a bit of additional evidence that such tumors arise from bronchial buds is the fact that epithelial elements have been reported in chondroma of the bronchus by McDonald, Harrington and Clagett,[43] a finding which we have confirmed in some of our own cases. Since the buds contain both endodermal and mesoblastic elements it might be expected that tumors arising from them would be composed of both elements. Just as the epithelial elements may give rise to a carcinoma, so malignant tumors may also arise from the mesoblastic components. Thus a fibrosarcoma may develop. Examples of that tumor have been reported recently by

Black[44] from our clinic, by Carswell and Kraeft[45] and by Curry and Fuchs.[46] Even more striking, however, is the occurrence of a combination of sarcoma and carcinoma in the same tumor. We have had two examples of the latter combination which will be reported by Bergman, Ackerman and Kemler.[47]

Although not arising in a bronchus there is another variety of primary carcinoma of the lung which should be mentioned briefly. It has been recognized only recently. It has been given various names of which the most commonly used are perhaps alveolar carcinoma, multiple adenomatosis and carcinoma mucocellulare. One of the most striking features of the condition is that it has a multiple origin. However, when the tumor is first recognized the multiple origins may all be confined to one lobe or one lung. The tumor arises in the parenchyma of the lung apparently in the cells lining the alveoli. The name "multiple adenomatosis" has been applied to the condition because sometimes one can recognize the multiple sites of origin as several nodules. The few cases which up to the present have been reported have either been uniformly fatal or apparently on the way to becoming so, with perhaps one exception. That exception is a case designated as a carcinoma mucocellulare and reported by Osserman and Neuhof.[48] After a lobectomy the patient was alive and well five years later. In three cases of my own one of the patients died within three years after lobectomy and another one slightly more than three years after a pneumonectomy. In the third case, although the patient is still living, less than a year has elapsed since a lobectomy was performed.

The condition is sometimes, but not always, characterized by the secretion of a large amount of mucus which may be coughed up by the patient and apparent also in the specimen of the tumor itself. Several case reports will be found in an article by Delarue and the writer.[49] Others will be found in articles by Drymalski, Thompson and Sweany,[50] by Wood and Pierson[51] by Stephens and Shipman,[52] by Swan,[53] and by Laipply and Fisher.[54]

A remarkable fact about this recently discovered tumor is that it seems to be identical in both gross and microscopic appearance, as well as its clinical course, to a disease of sheep known generally as "jagziekte." This name, a South African word, which means "driving sickness," has been applied to the condition because it was in South Africa that the disease was first recognized and carefully studied. It is now prevalent in

many parts of the world. In Iceland it occurs in epidemic form and is responsible for enormous losses of sheep. In recent years it has been recognized in the Western part of the United States. There seems to be rather general consent among pathologists who have studied this disease in the sheep that it is due to a virus which has not yet been found. Cowdry[55] was one of the pioneers in the investigation of the disease.

Summary

Bronchiogenic carcinoma has shown an amazingly increased incidence within the last thirty-five years and the increase seems to be progressive.

At the present time it is overwhelmingly a male disorder.

More and more evidence has been accumulated that excessive cigarette smoking is an important etiologic factor, although not the only one.

The great preponderance of the disease in the male sex is not due to any special immunity of females. Rather it seems due to the fact that, contrary to popular belief, many fewer women of the cancer age smoke than do men. A statistical study of this question demonstrates the truth of this statement.

The marked increase in bronchiogenic carcinoma has been in the type usually designated as epidermoid or squamous, or a variant recognized as a undifferentiated type.

A corresponding increase has not been noted in the adenocarcinoma or in those types which some pathologists call round cell or oat cell carcinoma.

Evidence is presented which seems to indicate that epidermoid carcinoma of the bronchus presents an entirely different etiology from that of adenocarcinoma, oat cell or round cell carcinoma. The suggestion is made that the former type of cancer is due to the metaplasia of adult to carcinomatous epithelium under the influence of one or more carcinogenic agents but that the adenocarcinoma, including the oat cell and round cell carcinoma, arises in a latent embryonic bronchial bud.

The recently recognized alveolar carcinoma, sometimes called multiple adenomatosis, which closely resembles the disease of sheep known as "jagziekte," is briefly discussed.

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NEWER METHODS IN THE DIAGNOSIS OF CONGENITAL CARDIAC ANOMALIES*

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DURING the last decade, studies of congenital heart anomalies have received great impetus, since corrective surgical procedures have been proposed for the treatment of the most common forms observed: Patent ductus arteriosus, coarctation of the aorta, pulmonic stenosis isolated or combined with other malformations, interauricular and interventricular septal defects. The selection of suitable cases for surgery has therefore become a clinical problem of considerable interest to practitioners who, in order to discharge properly their responsibility, should be well informed of new developments in methods of diagnosis.

In this lecture, I shall attempt to review our present day knowledge of two methods which have received widespread attention: Cardiac catheterization and Angiocardiography.

DISCUSSION OF METHODS

1. *Cardiac Catheterization*

The introduction of a long radio-opaque, modified ureteral catheter into the venous system under fluoroscopic control offers a means of sampling blood in the superior and inferior vena cava, in the right auricle, the right ventricle, the pulmonary artery and its branches. In a subject maintained in a steady state, variations in the oxygen content of mixed venous blood samples taken in rapid succession in these chambers and vessels are small. Abnormal communications between one of these right-sided structures and its adjacent counterpart on the left side of the heart, i.e., the left auricle, the left ventricle or the aorta, result

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in contamination of mixed venous blood returning from the tissues by well-oxygenated blood returning from the lungs, because the pressure conditions prevailing in the circulation favor blood shunts from left to right. Therefore, the approximate location of shunts can be determined by gas analysis of blood samples drawn through the catheter as its tip is placed in various right-sided cardiovascular structures. Moreover, the presence of an abnormal communication may be revealed by the unusual routes eventually taken by the tip of the exploring catheter as it is introduced into the heart.

Collection of arterial blood, through an indwelling needle, and determination of the oxygen content and saturation in the samples drawn may help also in recognizing contamination of well-oxygenated blood by mixed venous blood. Such contamination occurs when the dynamic conditions prevailing in the heart in the presence of a cardiac malformation, favor a shunt directed from the right cardiac cavities or the pulmonary artery into the left cardiac cavities or the aorta.

With simultaneous determinations of the oxygen intake into the lungs, and of the oxygen contents in the right heart and pulmonary artery, and of the oxygen content in a systemic artery, the calculation of blood flow in the systemic and in the pulmonary circuits and of blood shunts through abnormal communications, becomes a matter of applying simple formulas.

The technique of right heart catheterization provides also a means of recording blood pressures. The patterns of the curves and the range of normal pressure variations in the right and left auricle, the right and left ventricle, the pulmonary artery and the aorta, and in a peripheral artery, when tracings are obtained through an indwelling needle, are well defined. Hence, these blood pressure recordings may serve two purposes: 1) Identification of the cardiac cavities or large vessels in which the tip of the catheter is placed; 2) study of the effects of cardiac malformations upon the dynamics of the circulation.

Several conditions must be met if the results of cardiac catheterizations are to be considered valid and justifiable of an interpretation: 1) Blood samplings and pressure recordings must be made under fluoroscopic control. 2) Blood samplings, in the same vessels and cavities, must be multiplied and obtained in rapid succession. 3) A steady state of the respiration and circulation must be maintained during the whole period of samplings.

In young children, a general anesthetic may be required in order to maintain a steady state during the procedure. Multiple determinations of the oxygen saturation in blood samples may be facilitated and may even be instantaneously observed by the use of an oxymeter of special design. The blood pressure recordings must be made immediately visible, by means which depend upon the type of recorder in use.

Even though favorable technical conditions have been obtained, the interpretation of the data requires good judgment. The same differences in the oxygen content of the blood in two heart chambers may be due to different abnormalities. For instance, an increase in oxygen content in the right ventricle, as compared to the right auricle, in the presence of a patent ductus arteriosus, may be either due to pulmonary regurgitation or an associated interventricular septal defect.

The calculation of systemic or pulmonic flows and of shunts must be considered at best as an approximation, because it is not always possible to ascertain whether a sample obtained near, or even away from the main stream of a shunt, is adequately mixed with the rest of the blood flowing in the cardiac cavity or large vessel.

Most *complications* observed during and after cardiac catheterizations in the course of study of congenital cardiac anomalies, are of a minor character. Air emboli introduced into the catheter are potentially dangerous in cases where, hemodynamic conditions favoring right to left shunts, small air bubbles may be thrown into the systemic circulations. Precautions should therefore be taken to avoid introduction of bubbles into the catheter. A traumatic lesion of the endocardium with secondary thrombosis is another potential danger to be reckoned with. Although their frequent occurrence in the dog has been well documented, these lesions, to my knowledge, have been demonstrated in one single instance in humans, although they have been looked for by many investigators, when the occasion of doing so presented itself. Acute bouts of anoxia, following catheterization of a markedly stenotic pulmonary valve associated with an interauricular communication have been observed. Proper care should therefore be exercised in avoiding a prolonged obstruction of such a stenotic area especially when cyanosis develops, or its degree increases during manipulation of the catheter. Development of rhythm disturbances is by far the most important complication to consider. Since continuous electrocardiographic control has become a routine part of the exploration of the cardiac cavities and

of the thoracic great vessels, it has been found that ectopic beats, ectopic rhythms and tachycardias are not exceptional, and that conduction disturbances may develop, although much less frequently. The arrhythmias are more apt to occur when the tip of the catheter is in the infundibular area of the right ventricle, or introduced in the left ventricle through a septal defect. Save in exceptional instances they cease immediately upon displacement of the catheter, and have no clinical repercussion. But in the presence of prolonged bursts of ventricular tachycardia, one should fear a marked drop in systemic pressure which can in cases with cyanosis bring about a considerable increase in arterial anoxia and even more fear the development of ventricular fibrillation. Since the mortality rate attributable to this technique can be estimated from available figures at about two tenths of one per cent, it would appear that the risk is small indeed. It is nonetheless one that has to be taken into account before deciding to proceed with the technique.

From the preceding remarks, it is obvious that cardiac catheterization should only be undertaken by a well-trained team, in a well organized laboratory. The reliability of the results and the safety of the method depends upon meeting both these requirements.

2. *Angiocardiography*

Angiocardiography, as is well known, consists in the x-ray study of the cardiac chambers and thoracic great vessels during opacification by an intravenously injected radio-opaque solution. This method has been widely used in recent years for the diagnosis of various types of cardiac congenital malformations. With x-ray films of the chest taken in rapid sequence, it is possible to delineate the contour of the four cardiac chambers and of the large vessels, to visualize details of structures otherwise invisible, such as the valvular areas, and also to follow the order in which the cardiac cavities and large vessels are filled by the blood conveying this radio-opaque substance. Hence, details of abnormal anatomy, and unusual pathways taken by the circulating blood, may be revealed in the course of study of congenital heart anomalies, especially since x-ray exposure may be obtained now at the rate of several films each second in two different projections.

Introduction into the circulation of a radio-opaque substance, however, is not without some *risk*. In a very well documented paper, Dotter and Jackson have reported the result of a survey which revealed that

out of a total of nearly 7,000 angiocardiographic studies in 182 hospitals, twenty-six deaths had occurred which could be attributed to the injection of the radio-opaque substance. All but two of these deaths were observed in subjects with congenital heart diseases, most of them belonging to the cyanotic group. These figures indicate that angiocardiography is not to be undertaken lightly, and without sufficient indication in this type of patients.

Before analyzing the nature of the information supplied by both these new methods in the most prevalent forms of congenital cardiac anomalies, it must be emphasized that their results must be compared with, and often interpreted in the light of observations obtained by careful and exhaustive physical and x-ray examinations. Neither of these newer methods can be considered as a substitute for tried and sound clinical studies. Furthermore, coöperation between clinicians, roentgenologists and clinical physiologists is essential. It would be even better, in my estimation, if the clinician who is responsible for therapeutic decisions, could himself master these techniques, or at least be able to interpret their results and recognize their inadequacies.

Until the advent of these methods of exploration, advances in the knowledge of congenital heart disease has been relatively slow, and based essentially upon correlation between clinical observations and post-mortem examinations. Although the admirable achievements of Maud Abbott, J. B. Brown and Helen Taussig cannot be too highly praised, the anatomo-clinical method has in some instances created distorted views and false impressions. Cardiac catheterization and angiocardiography made possible a study of anatomic anomalies and dynamic processes in the living. Not only have they helped to discover that the incidence of certain malformations is greater than suspected, but they have added new significance to the interpretation of physical and x-ray signs, which to a great extent are expressions of these processes. Briefly, the introduction of these methods in the study of congenital heart disease has resulted in a sharpening of the diagnostic acumen of clinicians engaged in the study of these fascinating and often baffling cardiac anomalies.

Discussion of Results

1. *Non-Cyanotic Congenital Heart Anomalies*

We shall first examine the value and significance of data obtained

by cardiac catheterization and angiocardiography, in the most prevalent forms of the non-cyanotic types of congenital heart disease: Coarctation of the aorta; patent ductus arteriosus; interventricular and interauricular septal defects and finally, pulmonic stenosis, either isolated, or associated with a septal defect through which there is no reversal of the natural direction of shunt.

Coarctation of the Aorta: In coarctation of the aorta of the so-called adult type, a stenosis of a part of the aorta distal to the left subclavian artery is associated with hypertension in the upper extremities, and a lower blood pressure in the lower extremities, where the circulation is maintained as a result of the development of large anastomoses bridging the stenotic area.

Cardiac catheterization has no place in the study of such an anomaly, whereas the information obtained by angiocardiography can be considered as essential, and sometimes decisive in deciding the surgical approach.

The radio-opaque substance once it reaches the involved area, precisely delineates the nature and extent of the lesions. The left anterior oblique is the position of choice for the study.

As a rule one can easily recognize left ventricular enlargement; an ascending aorta slightly or markedly dilated; an innominate artery and a left subclavian artery greatly dilated; and a transverse aortic arch narrow and long. The site of the coarctation is identified as a short stub extending downwards and posteriorly beyond the subclavian artery, and appearing like the end of a sausage. The descending aorta usually dilated, overlaps slightly the stub, and as a rule, the opening between the two segments is not demonstrable readily. The timing of opacification of the descending aorta is *not* related to the size of the opening, but to the character of the collateral circulation. A pre-operative study of the site, length of the narrowed area, origin of collaterals, and of other branches of the arch of the aorta, permits as a rule the planning of the type of reparative surgery to be employed, especially whether a vessel graft should be available.

Rarely does angiocardiography fail to afford adequate demonstration of the abnormality. If it should fail, one may resort to retrograde aortography which consists in cannulating a carotid artery, or passing a long and narrow polyethylene tube up the aortic arch through a brachial artery, and injecting the contrast substance through the cannula or tube.

Potential dangers attendant to this type of exploration should limit its use to the exceptional case.

Patent Ductus Arteriosus: The persistent patency of a ductus arteriosus with continued communication between the aorta and the pulmonary artery results in a substantial volume of blood being shunted from the former into the latter, in accord with the large pressure difference existing between both vessels during the entire cardiac cycle. Hence the work of both ventricles, especially the left, and the pulmonary blood flow, are both increased. The large pulmonary blood flow together with increased pressure at the site of the shunt combine to cause the dilatation of the main pulmonary artery and of its major branches.

In most instances the clinical diagnosis is obvious, and the decision regarding surgical exploration arrived at without recourse to either cardiac catheterization or angiocardiography. However, in some cases the diagnosis may remain in doubt. This happens particularly in cases where a systolic murmur is present at the base with a collapsing type of pulmonary circulation as viewed by fluoroscopy; or when an additional systolic murmur is heard in the precordial area, or when the continuous classical murmur has its maximum lower than the second left interspace, and finally, when a diastolic murmur of pulmonary regurgitation complicates the picture.

Among the helpful information supplied by *cardiac catheterization*, one must list the direct demonstration of a patent ductus arteriosus by insertion of the tip of the catheter into this channel by way of the left pulmonary artery near its origin and the emergence of the tip in the descending thoracic aorta. Thus in left anterior oblique the opaque catheter appears as a cord subtending the arch of the aorta. An indirect demonstration of the shunt of well-oxygenated blood from the aorta to the pulmonary artery is provided by the finding of a considerable increase in the oxygen content in the latter vessel as compared to the oxygen content of the right ventricle and auricle.

Whereas analysis of the oxygen content in the successive blood samples obtained from the two right chambers and from the pulmonary artery cannot differentiate an aortic septal defect from a patent ductus arteriosus, the direct demonstration of the course followed by the catheter through the patent ductus is pathognomonic. However, the coarser character of the murmurs and thrills, their lower locations, a history of subacute endocarditis, are as a rule clinically suggestive of the

diagnosis of an aortic septal defect, a much rarer condition.

In patent ductus arteriosus, calculations indicate that as a result of the shunt, the pulmonary blood flow may reach two to four times that of the systemic blood flow. The blood pressures in the pulmonary artery may be normal, or sometimes considerably elevated, but there appears to be no absolute relationship between the height of pressure, the size of the shunt or the age of the subject. However, it must be borne in mind that as a result of prolonged or considerable increase in pulmonary blood flow atheromatous changes occur in pulmonary vessels, causing an increase in pulmonary vascular resistance which is reflected in a rise of pulmonary artery pressure, while as a result of this increased resistance, the magnitude of the aorta-pulmonary shunt diminishes. In some instances this process may lead to reversal of flow, and late cyanosis. In the presence of a complicating functional pulmonary valve incompetence which during diastole causes regurgitation of blood with a high oxygen content into the right ventricle, the average oxygen content in this cavity increases significantly above that of the right auricle. Under such conditions, the differential diagnosis on the bases of blood gas determinations may become difficult with 1) a high interventricular septal with persistence of laminar flow in the pulmonary artery, 2) a high ventricular septal defect complicated by aortic insufficiency, and 3) a combination of patent ductus arteriosus with an interventricular septal defect. Confusion, then, may result from the analysis of data obtained by cardiac catheterization, unless a very keen analysis is made of the character, location and propagation of murmurs present.

Angiocardiography is seldom used as a diagnostic procedure in patent ductus arteriosus. Several signs have been claimed to be of relative or absolute diagnostic value, i.e., 1) a localized dilatation of *the aorta* distal to the origin of the left subclavian artery, 2) enlargement of the pulmonary artery, with elevation of its left main branch; 3) reopacification of the left pulmonary artery at the time of the aortic opacification; 4) actual opacification of the patent ductus arteriosus.

Although the presence of the above mentioned localized dilatation of the aorta may be considered good presumptive evidence of a patent ductus arteriosus, it may occur in other conditions, and is often absent in proven cases. As for the actual opacification of the patent ductus arteriosus, it is exceptional unless the contrast medium is introduced by the method of retrograde aortography.

Interventricular septal defect: Two distinct locations of interventricular septal defects correspond to two distinct clinical and physiological pictures: 1) A simple perforation through the muscular part of the septum associated with characteristic discrete findings of the classical "maladie de Roger," with small volume of blood shunted from left to right, and a slight load placed on the heart which remains normal in size and shape. 2) A high septal defect located just below the semi-lunar valves which is associated with a large shunt, pulmonary hypertension, dilatation of the pulmonary artery, and hypertrophy of both ventricles.

Cardiac catheterization and *angiocardiography* are unnecessary in the first type, although the presence of the shunt may be demonstrated by gas analysis of blood samples, if it is of sufficient magnitude. In the second type, *cardiac catheterization* is of great help in demonstrating an increase in oxygen content in the right ventricle, particularly in the samples obtained in the infundibular area and the presence of pulmonary hypertension. As discussed previously the exclusion of the diagnosis of patent ductus arteriosus with pulmonary incompetence may present, even after catheterization, some difficulty.

Angiocardiography is of little use in this type of interventricular communication. If performed, it may occasionally show a persistent filling of the right ventricle and of the dilated pulmonary artery during left ventricular and aortic opacification.

Interauricular septal defect: The persistence of an ostium primum or secundum, or of a patent foramen ovale, allows blood to pass from one atrium to the other, the direction of the shunt depending upon the pressure relationship between both atrial cavities. Uusually, unless there is considerable dilatation of the right atrium, the shunt is predominantly from the left to right, as the pressures in the left auricle are normally higher than in the right, causing therefore an increase in pulmonary blood flow, and consequently, right ventricular enlargement and often dilatation of the pulmonary artery.

Cardiac catheterization may help demonstrate the presence of this defect either directly or indirectly: (a) Introduction of the tip of the catheter through the defect in the left auricle and into one of the pulmonary veins is easily recognized and usually, but not always, achievable. (b) The demonstration of a left to right shunt is based on the observations of a higher oxygen content in the blood sampled from the right atrium than in the mean value of blood oxygen from superior and inferior

venae cavae. Occasionally, if the tip of the catheter is at the time of blood sampling immediately in the path of the stream of highly oxygenated blood spurting from the left auricle, the demonstration of fully oxygenated blood becomes pathognomonic.

It should also be emphasized that in interauricular septal defects laminar blood flow may persist in the ventricle and even in the pulmonary artery causing variations in oxygen content in these chambers, especially when the shunt is large. This makes multiple sampling in this cavity and vessel essential in order to avoid confusion.

The pulmonary blood flow is sometimes greatly increased, reaching two to three times that in the systemic circulation, but may be also only slightly increased. Pulmonary arterial pressure which is as a rule normal or nearly normal, may be elevated occasionally and for no known reason.

The demonstration of an interatrial defect is of considerable diagnostic value in differentiating this malformation from others also associated with dilatation of pulmonary artery and with evidence of a large or even normal pulmonary blood flow. To the group with a large blood flow belongs the high ventricular septal defect, associated usually with high pulmonary arterial pressure; to the group with a normal, or nearly normal pulmonary blood flow, belong a variety of anomalies that we shall discuss shortly: Pulmonic stenosis of mild degree, Idiopathic dilatation of the pulmonary artery, and "Primary" pulmonary hypertension with pulmonary valve insufficiency.

As for the differentiation between an interauricular septal defect and direct drainage of a pulmonary vein into the right atrium, the solution depends upon the direction taken by the tip of the catheter, which in some instances may be revealing.

If and when *angiocardiography* is performed, x-ray exposure is preferable in the frontal view in adults, and in the left anterior oblique view in children. The films demonstrate a large right auricle, right ventricle and pulmonary artery, with engorged branches of the pulmonary artery, while the left auricular and ventricular cavities and the aorta are of normal size. Opacification of the right chambers and pulmonary artery persists after the left heart has been filled, but great caution should be exercised in interpreting this finding as a slow injection with pooling in the hepatic vein and jugular veins of some of the contrast medium may result in the same observation. In children the instantaneous spreading of the contrast medium from the right to the left atrium may be demon-

strated directly. This temporary reversal of flow through the defect is probably due to the temporary pressure increase in the right auricle, following the rapid injection of a fairly large quantity of liquid which has a small distance to run from the arm to the right auricle. Dotter and Steinberg estimate that with the multiple exposure technique this sign is present in about one-third of the cases only.

Pulmonic Stenosis: The problem of pulmonic stenosis not associated with dextroposition of the aorta, may be said to have been greatly clarified since congenital heart anomalies have been systematically studied by cardiac catheterization.

A. *Simple valvular stenosis and infundibular stenosis with closed septa* have been demonstrated in many instances. They are of two types, mild and severe, both characterized by pulmonary artery dilatation with normal pulmonary vascular markings. In the mild form, usually symptomless, there is no demonstrable right ventricular enlargement, whereas in the severe form, cyanosis of the peripheral type, i.e., not associated with arterial blood anoxia, breathlessness, and sometimes syncope and angina pectoris, may be observed. Evidences of right ventricular hypertrophy and dilatation with or without right ventricular failure, become more striking according to the degree of stenosis and the stage of evolution.

Cardiac catheterization provides characteristic findings namely a normal or low pulmonary arterial pressure associated with a moderate or considerable systolic hypertension in the right ventricle. The exact location at which the systolic pressure suddenly rises, when the tip of the catheter is withdrawn from the pulmonary artery into the right ventricle under fluoroscopic control, will help in differentiating valvular from infundibular stenosis. This information may be of considerable value, for a different type of valvulotomy may be used for the relief of each of these malformations. The oxygen concentration in all the samples removed from the right side of the heart and pulmonary artery, being nearly identical, closure of the septa is thus demonstrated.

In the mild form of pulmonic stenosis, the most common error made in differential diagnosis is that of suspecting an atrial septal defect with small shunt or a "maladie de Roger." In some cases with a mild degree of stenosis associated with an aneurysmal dilatation of the pulmonary artery, the only other diagnosis to be discussed is that of idiopathic dilatation of the pulmonary artery, where the systolic pressure in the right ventricle is not elevated, although the systolic pressure in the pul-

monary artery may be somewhat lower. In the severe forms of stenosis, confusion with any other conditions is unlikely as soon as it is demonstrated that the cyanosis is peripheral and therefore not associated with a reduction in the arterial blood oxygen saturation.

Angiocardiography is of little help, besides revealing the contours of the pulmonary artery and its main branches. Rarely does it demonstrate a narrow and irregular channel, either at the valve area or in the infundibular area. Great caution must be exercised in the interpretation of such details and cardiac catheterization should be performed if the diagnosis is in doubt.

B. *Pulmonic stenosis associated with septal defects but without reversal of blood flow* is also not an exceptional anomaly. The clinical signs of either the stenosis or the septal defect may dominate the course and the diagnosis may be puzzling.

Cardiac catheterization constitutes the keystone of the diagnosis in revealing both types of defects: 1) By supplying direct evidence of pulmonic stenosis derived from the blood pressure tracings and 2) a direct or an indirect demonstration of an associated septal defect by observations which have been previously commented upon.

Before we start a discussion of the use of these new methods in the cyanotic group of cardiac malformations, we may briefly summarize their essential indications in the acyanotic type:

1. *Cardiac catheterization* is especally important in subjects with enlargement or dilatation of the pulmonary artery, whenever the character of the murmur and thrill and other physical signs leave some doubt as to the exact nature of the defect, and when the surgical decision depends upon the accuracy of the diagnosis.

2. *Angiocardiographic studies* are indispensable in the preoperative study of coarctation of the aorta.

2. Cyanotic Types of Congenital Cardiac Anomalies

From the point of view of incidence as well as that of surgical interest, there are two major types of congenital heart anomalies, accompanied by cyanosis from early life on, namely (a) severe pulmonary stenosis with septal defect and reversal of shunt from right to left, and (b) severe pulmonary stenosis with a dextroposed (overriding) aorta which saddles a high interventricular septal defect.

Pulmonic stenosis with septal defects and reversal of shunt: Severe

pulmonic stenosis in the first of these anomalies causes 1) a reduction in pulmonary blood flow, but nonetheless a post-stenotic dilatation of the pulmonary artery is often present; 2) a considerable systolic hypertension in the right ventricle with hypertrophy of the wall of this chamber; 3) a dilatation of both right ventricle and right auricle with increase in the diastolic filling pressure. The later pressure rise results in a reversal of blood flow through the associated septal defect, usually interauricular or the patent foramen ovale.

As a rule, the clinical diagnosis is based on a history of rapid progression of a cyanosis which may have been mild at birth, and its association with a dilatation of the pulmonary artery. Since pulmonary valvulotomy rather than a Blalock anastomosis should be performed in this malformation, cardiac catheterization and angiocardiography are of great value in discarding the diagnosis of Tetralogy of Fallot. It should, however, be emphasized that the correct diagnosis may be strongly suspected on clinical grounds.

By *cardiac catheterization*, direct evidence may be attained of the presence of a pulmonic stenosis by pressure tracings. The systolic hypertension in the right ventricle is always considerable, reaching sometimes twice that in the peripheral systemic artery. Direct evidence of an interauricular communication is obtained, if the catheter tip may be slipped from the right auricle into the left auricle. It is notable that when there is reversal of flow through the interauricular communication, the oxgyen content in the right auricle, right ventricle and the pulmonary blood samples are identical.

Angiocardiography reveals (a) an early shunt of blood from the right auricle to the left auricle by simultaneous filling of both these cavities, (b) an early opacification of the left ventricle and aorta, (c) a minimal opacification of the right ventricle and of the dilated pulmonary artery, (d) a late reopacification of the left auricle. All these findings are of great diagnostic value. Occasionally, the character and location of the stenosis may also be revealed.

In exceptional cases, a severe pulmonic stenosis is associated with an interventricular septal defect with reversal of shunt. This diagnosis will be considered, in the discussion of the classic Tetralogy of Fallot, where in addition dextroposition of the aorta is present.

Pulmonic stenosis with dextroposition of the aorta (Tetralogy of Fallot). Combination of these two defects, pulmonic stenosis and dextro-

position (overriding) of the aorta, underlies the most common types of congential cardiac malformations with cyanosis present since birth.

The overriding of the aorta implies of necessity a high interventricular septal defect; the semi-annular form of this defect is distinct in general from the annular form of the isolated high septal defect previously depicted. The right ventricular hypertrophy constitutes the fourth element of the classical Tetralogy of Fallot, under which title this group of anomalies are best known. The degree of ventricular hypertrophy which is most likely dependent upon the degree of pulmonic stenosis and of dextroposition of the aorta, is variable, but never reaches that which is seen in some cases of isolated severe pulmonic stenosis. The anatomic and physiologic variants of this type of anomaly are numerous. They are dominated by 1) the degree of stenosis which may range from a slight narrowing to complete atresia and 2) by the degree of overriding of the aorta which may vary from slight to extreme. Dynamically each ventricle may maintain its identity, or both may function as a single ventricle. The distinction between specific types such as classic Tetralogy of Fallot, pulmonary atresia, pseudotruncus arteriosus, extreme dextroposition with common truncus, where some degree of oxygenation of blood in the lungs is maintained, mainly by the markedly dilated bronchial arteries, is not only of academic interest, but also of practical value, since some clinicians consider that pulmonic atresia is a contraindication to a Blalock-Taussig type of operation, and since all agree that the operation is not physiologically feasible in Common Truncus. The respective amount of blood flowing through the pulmonary artery and its branches, and through the aorta, is determined primarily by the respective resistances to flow at the site of the stenosis and in the entire aortic system. As a rule the flow through the main pulmonary artery is considerably reduced, or even absent, as in atresia—in mild form of stenosis it may occasionally be as large as in the aorta. It also stands to reason that the degree of arterial blood oxygen unsaturation and therefore, of cyanosis, is determined by the amount of mixed venous blood shunting directly into the overriding aorta.

The clinical diagnosis is as a rule simple, when the physical signs and x-ray findings are according to the classical description. The exact diagnosis may, however, require special investigations, in particular when (a) the cyanosis is only mild, (b) a post-stenotic dilatation of the pul-

monary artery is present, (c) the reduction in pulmonary blood flow is small, (d) pulmonary atresia with considerable collateral circulation is present. These studies are primarily directed at demonstrating preoperatively whether palliative surgery is indicated and if so, to give advance information concerning choice and modality of techniques to be employed.

In the course of *cardiac catheterization*, the probing tip of the catheter as it progresses into the right ventricle may directly demonstrate the overriding aorta. In such instances, it is seen progressing into a right or left arch, and descending aorta. Pulmonary stenosis may also be demonstrated, if the catheter is introduced into the pulmonary artery by recording pressure tracings. Whereas the pressures are low in the pulmonary artery, the systolic pressure is elevated in the right ventricle, to a varying degree and sometimes attains the systolic pressure level measured in the aorta, or in the systemic artery. The oxygen contents in the blood sampled from the right auricle and the right ventricle and even the pulmonary artery, may be the same when the amount of shunt from the left ventricle to the infundibular area is insignificant. Not uncommonly, however, evidence of some small degree of left ventricular blood shunting appears in this latter region of the right ventricle. Samples of blood collected in the aorta or in a peripheral arterial blood, although more or less unsaturated with oxygen, have always a higher saturation than the right ventricular blood. This evidence helps to exclude the diagnosis of total transposition of the aorta, where the vessel originating from the right ventricle, has the same composition as the right ventricular mixed venous blood. In cases of atresia, or pseudo-truncus arteriosus, where the tip of the catheter cannot be introduced in the pulmonary artery, the degree of blood oxygen unsaturation in the aorta or a peripheral artery, is always considerable, but less so than in the right ventricle. Moreover, it must be strongly emphasized that failure to catheterize the pulmonary artery is no proof of the presence of an atresia. Similarly, failure to introduce the tip of the catheter into the aorta, cannot be given as an evidence that there is little or no dextroposition of this vessel.

Angiocardiography demonstrates superbly the essential defect by simultaneous opacification of the aorta and pulmonary artery, at the time of right ventricular opacification. This picture is almost pathognomonic and quite distinct from that observed in a single ventricle,

where the entire ventricular cavity and both large vessels are opacified simultaneously. The site of the stenosis may sometimes be difficult to demonstrate, but a poor pulmonary vascular filling is a sign of a reduction in the blood flow in the pulmonary artery. In the case of atresia, aortic opacification takes place alone without opacification of the pulmonary vessels. It is exceptional in this malformation to be able to visualize clearly the bronchial vessels, as they branch off the aorta.

Dextroposition of the aorta without pulmonary stenosis: Dextroposition of the aorta may sometimes develop without concomitant pulmonary stenosis. This anomaly has been much discussed in recent years under the heading of Eisenmenger complex. From the experience gained by the use of the new techniques of diagnosis it would seem that the incidence and the importance of this syndrome has been greatly overrated.

In its typical form the complex is characterized by the shunting of a large amount of left ventricular well-oxygenated blood, through an interventricular septal defect, into the pulmonary vascular system where normally resistance to flow is lower than in the aortic system. This results in a large increase in pulmonary blood flow, and the pulmonary artery becomes markedly dilated. The amount of mixed venous blood flowing directly in the overriding aorta is usually small, and therefore, cyanosis is minimal or absent, although the arterial blood oxygen saturation is always slightly reduced. However, under hemodynamic conditions not always well defined, the resistance in the pulmonary vascular bed may increase to such an extent that left to right shunt is progressively reduced, as the pulmonary arterial pressure increases, and mixed venous blood shunts from the right ventricle to the dextroposed aorta. It is in such instances that the dilatation of the pulmonary artery associated with a reduction in the pulmonary blood flow and with increasing evidence of contamination of the arterial blood by mixed venous blood creates a picture which simulates (a) a Tetralogy of Fallot with mild pulmonic stenosis and post-stenotic dilatation of the pulmonary artery; (b) a high interventricular septal defect with considerable pulmonary hypertension and reversal of shunt; (c) an idiopathic pulmonary hypertension with reversal of blood flow through a patent foramen ovale.

Catheterization of the heart is of great diagnostic value if it simultaneously demonstrates: dextroposition of the aorta, absence of pulmonic stenosis, and identical systolic pressures in the pulmonary artery,

the right ventricle and the aorta.

The *angiocardiographic findings* of a simultaneous opacification of the pulmonary artery and aorta, although suggestive, is not diagnostic, as it may be present in all the anomalies under discussion.

To summarize the indications of cardiac catheterization and angiocardiography, in the most prevalent forms of cardiac congenital anomalies of the cyanotic group, it may be stated that both are of great diagnostic value, especially the latter which according to Dotter and Steinberg should be performed routinely in all cases considered for surgery.

Conclusion

Since the introduction of cardiac catheterization and angiocardiography in the study of cardiac congenital anomalies, additional diagnostic information has been gained. Many physical and roentgenologic signs have acquired new meaning and significance, so much so that clinicians familiar with these new techniques feel that they have become unnecessary in many instances. In this presentation an attempt has been made to formulate clear-cut indications for the use of either or both methods. However, because their use entails a minimal but definite risk, especially in the hands of the neophyte and of the daring, a note of caution has been sounded and it has been stressed that good judgment should always be exercised and instantaneous electrocardiographic control should always be available in the course of cardiac catheterization. A further conclusion should emerge from this discussion, i.e., that only those cases should be studied where the diagnosis after careful and expert clinical examination, is still in doubt, and if a better documented diagnosis may be of aid in reaching a therapeutic decision. To the credit of these new methods stand foremost 1) a truer picture of the clinical incidence of some defects which are justifiable of surgery and 2) the considerable progress which has been achieved in the understanding of the physiopathology of the various defects, and of their influence upon the dynamics of the circulation.

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AN APPRAISAL OF PSYCHOANALYSIS FOR THE PRACTITIONER*

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To give an appraisal of psychoanalysis for any group of people is a large order. It is a subject with which the New Yorker deals more graphically and the movies more spectacularly than a lecture possibly can. Beside them, it will be dull and dry, but more accurate. It is obvious, too, that in an hour's time it is scarcely possible to make a complete evaluation of psychoanalysis,—either to criticise or appreciate its scientific method, to evaluate it as a therapy, to state the main theoretical principles which have evolved from its investigations, or even to give a fairly full account of its history. Since this is a lecture for medical practitioners, it will attempt to discuss some of the practical aspects of psychoanalysis, its applications and its limitations—in the hope that this may be useful and somewhat interesting.

The story is now well known of how an Austrian physician, Josef Breuer, himself a busy practitioner paying attention to the talk and behavior of an hysterical woman patient, developed the idea that her symptoms were the result of certain emotional experiences and impressions arising during the course of nursing her sick father. He treated her with hypnotism as was the custom of the day, but instead of giving her the ordinary sort of hypnotic therapeutic suggestions he urged her during the hypnotic trance to search for the connections between the original experiences and the current symptoms, and to relive fully in this new situation the older experiences. Following this the patient's symptoms were very much ameliorated. This was the faint beginning of psychoanalysis. Breuer confided his investigations in his young colleague, Freud, who some years later (in the early 1890's) returned to work with Breuer and take over the treatment of some of the neurotic patients who formed, then as now, an appreciable and perhaps trying

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part of the older man's practice. In 1895 they published together "Studies in Hysteria," which was the beginning of Freud's long series of publications concerning his investigations, to which he subsequently gave the name of psychoanalysis. This is used both to mean "a particular method of treating nervous disorders and also the science of the unconscious mental processes, which has also been appropriately described as 'depth psychology'."*

The word *unconscious* here slips into the discussion, a word which may in general parlance have a number of different shades of meaning, from a state of unawareness or lack of deliberation to a state of coma. The *unconscious* as understood by the psychoanalyst refers to psychological processes present and active in all human beings, but of which the individual himself is unaware. We are used to thinking of ourselves as rational, deliberating, logical creatures, whose capacity for reason and thoughtful memory marks us as vastly superior to our four-footed colleagues. Yet we do many irrational and foolish acts without being aware of what drives us to do them, or we explain them on spurious, slight and quite inadequate bases (i.e., we rationalize them), satisfying ourselves but not others of the reasonability of our performances. It is the belief of psychoanalysis that in many mental disturbances the symptomatic behavior due to these unconscious forces cannot be modified in any nearly permanent way, unless the individual becomes aware of the nature and source of his unconscious drives and motives, i.e., the content of unconscious processes is then made conscious and the behavior is reshaped and made more appropriate. This making conscious of what in himself has previously been unknown to the patient is naturally a painful and disturbing process, but it increases his command of himself, and when effected gives a genuine self possession, and greater, rather than less, responsibility for the self. This is, of course, an overly simplified schematic account of the main therapeutic work of psychoanalysis, but it is not possible to give here more than the barest outline. It is true too that in the process of revealing the unconscious processes, many of their more destructive influences are modified. Thus in the course of psychoanalysis, the individual learns more fully about the disturbing elements in himself so that he can cope with them better consciously, and in the process of learning he modifies them somewhat.

The source of the greatest trouble from the unconscious seems to be

* Quoted from article on Psychoanalysis by Freud in the Encyclopedia Britannica.

in the powerful biological instincts with which we are equipped and their derivative drives, and from special painful situations and experiences of childhood in which they are aroused. I would mention especially sexual and aggressive instincts, which may be aroused inappropriately and with frightening results. It is in general our tendency to forget or repress those experiences which are disturbing to us, in our natural effort to maintain a reasonably pleasant equilibrium. Any one who scrutinizes himself carefully after some particularly humiliating or painful experience, particularly if it involves guilt or shame or loss of self-esteem, will see how he gradually detoxicates this experience, explains it away, by playing up excuses, blaming others, or shutting the door on it, i.e., making a fairly rapid exclusion of it resulting in a quick modification or forgetting. Such experiences, even when "completely forgotten" are not always inactive and not eliminated from a place in the inner psychic structure of the individual, but only from his specific awareness (conscious memory) of them. They exert forces of their own, generally in circuitous ways. The individual may guard against reactivation of the memory by building up self-protective character traits or by other lines of defence. Thus the original experience may be visible chiefly through having produced excessive reactions in the opposite direction, like excessively strong walls sequestering an unruly and troublesome prisoner. Such walls may in the end become irksome and restricting themselves, and in psychic disorders, as well as in physical ones, the symptoms may arise from the defences of the organism as well as from its threatened destruction. More commonly, however, the unruly prisoner does not die or become moribund, but the forces that have created him at first continue to assert themselves, while there is a constant counter force exerted to keep them in check. This is a vulnerable and energy-consuming state of affairs, and when a new situation arises somewhat similar to the first, the encapsulated forces (which I have dramatized as the prisoner) are rearoused and strengthened, the individual feels threatened from within, without knowing why, and develops symptoms of anxiety or nervousness.

The greatest sources or roots of disturbance arise in early childhood. This is perhaps the penalty of our high psychobiological development and the consequent prolonged helplessness of the human infant and child as compared to that of the young of other species. The child, in his dependence on an adult world, may be aroused to overly strong

and misunderstood emotions which seem to threaten him unduly, and he may also suffer fear of outside forces against which his limited strength is useless. These experiences set up patterns of emotional expectation and attitudes, often not consistently useful or appropriate, which tend to reassert themselves in a repetitive fashion later in life without the realization that there are other possibilities. It is only when the nature and source of such repetitive attitudes is brought clearly into consciousness in adult life, when the individual is no longer in the same helpless situation of childhood, that the older patterning of childhood is broken and the capacity for autonomy of the adult interferes, modifies, or takes over.

It has been mentioned that Freud and Breuer began their work with hypnosis. This was before long replaced by other and more fruitful ways of reaching the unconscious; namely, through the analysis of dreams and through the use of free association. By free association is meant the verbalization of the apparently loosely associated thoughts which pass through the background of the mind in a state of relative relaxation. In contrast to directed, logical thought, with which we are wont to attack most of the specific problems of work, free association produces thoughts with emotional rather than intellectual connections. The patient is directed only to say without censorship and as simply as possible those thoughts which pass across his mind. Thus are obtained certain inner connections between ideas based on feelings more nearly as they really work, rather than as the person would like to believe they work. Thus underlying motives and emotional drives of which the patient may be unaware may be revealed to the physician whose ear is sensitive and trained.

The use of these avenues to the unconscious rather than the quick direct highroad of hypnosis was especially valuable in that it permitted conscious rapport to be maintained between physician and patient even at the same time that the contents of the unconscious were being brought out. Thus such contents could be not only revealed, as with hypnosis, but worked with, through the patient's being brought to see repeatedly the unfruitful or positively destructive impingement of the past on the present, and what particular stimulating current situations were evoking the older repetitive but incompletely appropriate reactions. It is not possible in this brief presentation to say much in detail concerning the analysis of dreams. The elucidation of the economical

functioning of dreams in the life of the individual, their extraordinary condensation of past and present, the way in which they represent the storehouse of all memory, all this seems to me the most astoundingly valuable work of the genius Freud.

There is one other major tool of psychoanalysis which should be described briefly—viz., the relationship of analyst and patient. This is designated the *transference relationship* for reasons which will presently be mentioned.

Our reactions in everyday life are comprised in varying proportions of the realistic, appropriate responses to current stimulating situations plus the attitudes which have already been developed by earlier reactions to similar or related situations. These latter may in large measure be unconscious. In psychoanalytic treatment the analyst remains as far as possible anonymous and neutral in his personal relationship to the patient. Contrary to the belief of many, it is neither necessary nor advisable for the analyst to impress his patient with his personality, or to advise, direct, or exert the influence of suggestion. Ideally, he serves rather as an agent for clarification to the patient, the intermediary between the patient and his own unconscious. Thus there is set up in analysis an artificial situation, not reproduced anywhere else in life, in which the relationship between two people is as nearly as possible for the benefit of only one of them, the patient. For this reason the analyst must forego social or other contacts with his patient and (New Yorker cartoons to the contrary) reveal himself as little as possible to his patient. Their only relationship is the analytic one-sided one. Under these conditions, the stimulus from the analyst remains minimal, while the patient in revealing himself gradually develops emotional reactions which reproduce earlier ones toward members of his family, chiefly his parents, i.e., the patient transfers to the analyst emotional attitudes which have nothing to do with the actual situation but arise from the remote past, or are displacements from the present. The tendency to produce transference reactions focussed upon the analyst is particularly strong in those suffering from neuroses. The transference relationship thus becomes a valuable medium of investigation of the patient's troubled emotions, and must be jealously guarded from present infringements and contaminations.

This presentation would be both grossly incomplete and disappointing if it failed to take cognizance of the importance of the sexual de-

velopment of the child's early years and of the Oedipus Complex. The early work in psychoanalysis indicated that the sexual instincts manifest themselves, not merely after puberty, but in the first years of life as well, during which they go through a progressive development reaching a height at about five years. In fact, the sexual life reaches two peaks, the first occurring at the age of five, and the second at puberty. Between these there is a period of relative latency. This double onset of sexual development, paralleled in the development of the sexual organs themselves, is characteristic of man in distinction to the other animals, and may be biogenetically determined.

The first period of sexual development (until the age of five), although naturally doomed to frustration and biological ineffectiveness, is of the greatest importance to the individual. The experiences of this period both in regard to the sexual and the aggressive drives, give rise to nuclear emotional patterns of attitude and expectation deeply rooted in the developing character, and shaping the future personality. These infantile patterns emerge again with sharpness during the propulsive growth of puberty, when they may be modified to a varying degree. The vicissitudes of development of the first years are of especial significance in the development of neuroses, in which certain early pivotal points of fixation (premature organization) may have remained uncorrected and, by repetition or increment, or by forming the nodal points of overly developed self protective attitudes, produce the symptoms of the later neurosis or personality deformation.

It is possible that this early period of sexual development, which is a less developed form of the later mature biological development, represents ontogenetically some early period in man's development. The sexual drives of these early years are naturally played out on the parents and siblings, and are inevitably doomed to frustration, thus universally giving rise to childish conflicts, the strength and variations of which (rather than the actual occurrence) are important in determining the neurosis. The most important (universal) developmental conflict of this period has been designated the *Oedipus Complex*, since the Greek mythical tragedy of that name portrays strikingly the constellation of the intra-family emotional forces which is so characteristic of the disturbed outcome of this period of infantile sexual frustration. In the healthier solution of this conflict, there is a reallocation of the energy previously involved in the child's sexual drives to the unsexual aims of

learning and social activities, and a strengthening of the sense of mastery of self, with a beginning formation of healthy ideals and anticipations. It should be realized that the child's sexual interest at its height, although associated with actual (primitive) genital feelings, is in certain respects different from the adult's, and that the reaction to these drives goes through another re-shaping in the growth and struggle of puberty.

Psychoanalysis did not meet with a ready reception, and perhaps least of all from the medical profession. This was inevitable. The uncovering of the importance of sexual drives in childhood and the emphasis on work with unconscious motivations are the two areas which offend people generally. Since we have had to be frustrated in our impossible childhood wishes, it is disturbing and painful to us to be reminded of this. We prefer to believe that that which is forgotten is lost, rather than that it lives on in us with a varying degree of active pressure. It is easier to think that conscious memory is the only valuable memory, or perhaps the only form of memory at all. Similarly, it offends our self-esteem and our estimate of our nobility and of our capacity for intellectual thought to realize that we are also moved by unrecognized and sometimes quite primitive forces within ourselves. When these break through to outward manifestations in "blind" emotional states, disproportionate rages, states of despair, or other excitements that arise with slight or trivial provocation, then we recognize that the individual is mentally sick or morally bad, but it is hard to accept that we ourselves have in any degree the same potentialities.

The development of psychoanalysis at the end of the 19th and the beginning of the 20th Centuries, just at the close of the Victorian era and following a rich and productive period of medical research in physiology and anatomy, with an emphasis on the body as a machine, probably lent cultural support to the antagonism which would be inherent anyway in people's attitudes toward their own instinctual drives. It was a period in which we of the "enlightened" part of the world regarded war as disappearing and an improbable event in the future, overstressed the advantages of mechanical inventions, and spoke as though they would liberate us, not always recognizing that they are but extensions of ourselves and utilized, like the machines of our bodies, as agents of our emotional drives. Morality, social awareness, codes of behavior, from rules of etiquette to legal statutes, were expected to take care of

our emotionally driven behavior, sometimes with procrustean demands and again like an old shoe which we were used to and could wear with comfort. It was an era in psychiatry in which mentally sick patients were still grouped with criminals and paupers in some localities, and housed, when their behavior was too disturbing, in almshouses and jails. This was not true universally, but the main care of the mentally sick was one of isolation, separation from society in massive hospitals called asylums. Psychiatry, since it dealt so largely with the irrational, was inevitably then the step-child of medicine, which was emerging with its spectacular researches. There had already developed in the more advanced areas an effort at a descriptive, morphological approach to mental disorders, and attempts at classification, largely according to external behavior and not according to dynamic functioning, except so far as this could be understood in terms of the current neurological research and the concept of brain localization which soon became extensively and enthusiastically over extended, with its offer of the security of definiteness and precision.

Psychoanalysis, which started as an empirical therapy for the neurotically ill, after a time opened the way to an understanding of the normal as well as malfunctioning psyche. It became not merely a technique of treatment, but a science. From the treatment of the ill, much was learned first of pathological and then of normal development. It is probably true that the effect of psychoanalysis at present is much wider than the benefits to the relatively small group of patients who have been treated by it; since its broader contribution has been due to the increased understanding of the problems of the development of children and of human relationships, and the infiltration of this into education, sociology, criminology and more recently into medicine.

The Limitations of Psychoanalysis

In contrast to the broad diffusion of psychoanalytic thinking are the limitations of psychoanalysis as a technical procedure.

It will be noted from what has already been described that the psychoanalytic method emphasizes the autonomy of the patient – that the analyst does not direct, suggest or persuade the patient to any course of behavior, but leaves it strictly to the patient to make his own decisions, for which he must also accept responsibility. Analysis rather makes the patient aware of the nature and motivations of his present

acts, at the same time relieving him to a considerable extent of the tensions of his patterned reactions of the past, but it does not prescribe a course of action for him. (In this way it differs conspicuously from educational or guidance types of psychotherapy.) This means in itself that the patient must have a sufficiently sound core of development both intellectually and in his ego (his sense of himself) so that he can accept responsibility and autonomy. Thus it is most useful in the neuroses and is not generally applicable to psychoses or certain types of severe disorders of character. It is true that in some severe and borderline cases it may be used by especially skilled therapists who devote some time to building up the ego of the patient by psychotherapeutic methods before even a modified analytic technique is begun; and some experimental work is now being done in beginning therapy of this kind in non-autonomous psychotic patients – i.e., those who are so sick that they have to be hospitalized at least temporarily, and are not fully in contact with reality. In general, however, psychoanalytic treatment is most available to patients who have a capacity for self direction in the ordinary activities of life and have sufficient contact with reality to be able to live and work in the community, although suffering from neurotic symptoms. The treatment is time consuming, to the extent of an hour daily (usually five times a week), and it may last for months or even, in severe cases, several years. It is a slow method, since it involves meticulous, patient rooting out of old pathological attitudes, while allowing a new developmental growth to take their place. It is usually not enough for us to know the general outlines of our disturbances; for a real relief of tension and anxiety from older sources we need to track down the disturbance to the specific situations where it arose.

The expense of this treatment is often cited as one of its limitations. I am not so impressed with this as many are. It is expensive to be sick in any sphere, and any treatment involving extensive reconstruction will of course be expensive. When one considers that many patients who can be treated successfully by psychoanalysis would progress otherwise into more disabling neurotic states, incapacitating them in earning a livelihood, or causing panics requiring hospitalization, psychoanalysis is *not* expensive, and more than pays for itself by enabling patients to continue work who would otherwise suffer loss of work, self esteem, and sometimes ultimately self direction. The expense of psychoanalysis

is not always readily borne, for it means a definite financial commitment over a period of time, which is neither as heroic nor as dramatic as an emergency operation or other critical procedures, and it is often some time before any improvement will be noted. Where the expense of psychoanalysis appears to be the severest limitation is among young people of the professional and so-called white collar groups, who have as yet very limited incomes, but whose development may be cramped by neurotic inhibitions or symptoms. In recent years, however, treatment at nominal fees is gradually being made available to such patients through out-patient services connected with psychoanalytic training centers. These can as yet serve only a very few of the many patients who apply for treatment, but they are a beginning which may develop considerably.

Further limitation of the application of psychoanalysis as a therapeutic technique lies in its being applicable only in certain eras of life. It finds its best subjects in the third and fourth decades of life (from twenty to forty) although it is frequently used also in the forties, and very rarely at later years. It is desirable that the analytic subject be old enough to have a reasonable capacity to make his own decisions and accept his own responsibilities and a sufficient strength to bear the pain of facing the depths of his own problems, and it is necessary that there be sufficient time left in life for the post analytic growth to take place and give new ways. It is not easy to set time limits to the selection of patients, as one person at 50 is more plastic and workable than another may be at 30. Thus the rigidity of the basic personality is a factor to be considered along with the actual age in deciding in a given instance whether the patient's condition is one favorable for psychoanalytic treatment. A modified form of psychoanalysis is used in the treatment of children, for the strict analytic technique can obviously be used only in adults.

To a certain extent cities, rather than smaller communities, are favorable for the practitioner of psychoanalysis. This is due to the need of the analyst to remain apart from social or other relationships with his patients and with members of their immediate families or close friends, lest such contacts vitiate the clearness of the transference relationship. This, however, is a limitation to the analyst, and secondarily then to the patient.

Another of the limitations of psychoanalysis is the relatively small

number of people who are trained and the amount of time necessary for the sound training of a practitioner in psychoanalysis. This is a state of affairs which changes gradually, however, and the last five years have seen a proportionately large increase in the number of trained psychoanalysts. The war, with its relatively large number of neurotic casualties, undoubtedly focussed the attention of many young doctors on the need for training of this kind and increased many times the number of applicants for training.

The Training of a Psychoanalyst

Is a rather prolonged and arduous affair. Not everyone is well suited temperamentally for this. There is a special type of sensitivity, a capacity for empathy with the sufferer, and a patient tolerance, which is essential in the psychoanalyst, in other words, a special type of psychological aptitude. The analyst must be willing to forego the rewards of friendships with his patients, in general to keep himself inconspicuous in the community, to tolerate being passive and anonymous, and to take with impersonal equanimity the 'unjust' transference reactions of his patients, and the misunderstanding of his acquaintances. Naturally, there must be a compensation in the interest in the work itself. He should be a person of integrity, capable of keeping confidences unflinchingly and resisting completely any temptation to use his association with his patient for any ends whatsoever except the investigation of the patient's disturbances. The formal training requires that the analyst be a physician with at least basic medical and psychiatric hospital training. The specific training in psychoanalysis is three-fold: the personal analysis of each prospective analyst; supervisory training in the analysis of his own first patients (comparable to clinical supervision in any other branch of medical therapy); and a prescribed curriculum of courses dealing with psychoanalytic theory and methods. The entire course of special psychoanalytic training generally is spread over a period of three to five years.

The personal analysis of the analytic student is essential and the corner stone of later training. This might at first glance seem an odd requirement. We do not ask surgeons to be operated on before they practice on others, nor internists to take their own medicine, although privately we may think that it would conceivably add to their understanding of their patients if they did happen to have these experiences.

With the analyst, however, this taking of his own medicine is necessary. Not only does the analytic student thus learn most effectively by studying the unconscious mental processes in himself before he works with them in another, but through his own personal analysis he is relieved of the tensions which would otherwise be aroused in him by the impingement of the problems of his patients on himself. The working of the unconscious is rather tricky and unless the psychoanalyst has been made aware of his own problems and their unconscious roots in himself, he runs the risk not only of increasing tensions in himself, but of doing injustice to his patients through incomplete vision of them in the areas where his own repressions interfere, or on the other hand, indulging in excesses of zeal if he is unconsciously attempting to solve his own problems vicariously through his patients. There was a time when it was believed that a prospective analysist needed only so much personal analysis as would bring him to a speaking acquaintance with the working of his own unconscious processes. Rather generally now this point of view has given way to the belief that a rather thorough preliminary analysis is desirable and perhaps essential, for the reasons I have mentioned.

How Effective Is Analysis?

This is a question which is asked periodically with considerable vehemence, both by analysts and by their medical colleagues. It is a question which I myself am not prepared to answer. To me it seems that so general a question as this loses much of its significance. One might almost as well ask "How effective is surgery?" It is rather a question of "In what types of cases is it effective?" and "In what way?" As new techniques are devised and tested out, as is now being done in the treatment of psychotic patients and in certain of the physical disorders in which emotional factors are prominent, so also there will at first be more failures in some areas. This is the history of a developing science. Psychoanalysis is a complex technique, not to be compared in content or statistically with such therapeutic procedures as the use of antibiotics, complex as they are. Neurotic disorders are far-reaching. If we are cautious and not zealous to prove a point either for or against psychoanalysis, we must be content to study long term results and a large number of cases, and to study results with careful scrutiny of what has actually happened in each instance, not merely with a tabu-

lation of this or that symptomatic state. This is a problem of all psychiatry, not limited to psychoanalysis. It may in the future be possible to set up some research study on therapeutic processes in psychoanalysis which will be discriminating and useful, through the pooling of case studies in treatment centers, but this has not so far been feasible.

Research Values

Psychoanalysis started as a therapeutic technique, which by its very investigative nature led in the course of time to essential contributions to dynamic psychology and psychiatry. Through the reconstructions of early life much was learned of the development of the human psyche both in normal and in disturbed states. It is noteworthy that many aspects of the theories of development arising from analytic reconstructions have since been supported by independent observations in allied fields. We might say that the first research contributions of psychoanalysis were in its own field and the adjacent fields of psychology and psychiatry. That psychoanalytic concepts lent much to the understanding and handling of problems of morale, shock, traumatic neurosis and other psychopathological problems of the last war was amply evident, even though such conditions were not treated by the technique of psychoanalysis, i.e., the understanding of psychoanalytic principles aided in understanding and in devising emergency treatment necessary under war conditions. There is at present a constant investigation of shorter treatment methods based on understanding of the unconscious and especially suitable for certain groups of patients or under special conditions.

I must pay my respects to the contributions of psychoanalytic research to education, to sociology and to anthropology, though I am not sufficiently informed in these fields to speak with a critical specificity.

Before closing, however, I would speak briefly of the coöperative research efforts between medicine, psychiatry and psychoanalysis which are now so widespread. These may for convenience be divided into three groups: 1) The understanding of the importance of the patient-physician relationship in the handling of medical problems. This is not identical with, but has some relation to the transference relationship of the psychoanalytic procedure. 2) The understanding of the patient's unconscious as well as conscious reactions to illness, for example, in

what ways any illness may reactivate earlier traumata or threats of body injury, and thereby set in motion anxieties from hidden sources; or the opposite situation where the illness reinstates an old dependency which may, if unrecognized, lead to unnecessary prolongation of convalescence or to an actual secondary invalidism. I cite these merely as illustrations among many which might be given; 3) the investigation of the direct effect of emotional conflicts on body states at different levels of development;—the origin of special and varying patterning of bodily concomitants of anxiety and their sequelae in physical as well as in psychological health; the body-memory deposit of physical and emotional experiences early in life when expression of emotion and relief through communication is limited; the selection of one body system or another for expressions of tension and emotional conflict according to early experiences of overstimulation or frustration to which the child is subjected (e.g., the simplest examples—feeding frustrations leading to gastro-intestinal sensitivities, excessive use of enemas leading to lower bowel tensions; suppression of pathological rage with resultant muscle tensions, etc.); and the coöperation of such conditions with special problems of inherent body constitution. There is a rich and conflicting body of observations in these areas, indicating activity and interest in a new frontier, out of which we may ultimately expect precipitates of considerable value.

THE USES AND ABUSES OF ANTIHISTAMINE DRUGS*

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EARLY last year a drug manufacturer estimated that one hundred million dollars worth of antihistaminic drugs would be sold during 1950![1] Whether or not this prediction proves accurate, it emphasizes the fact that these drugs are being used in tremendous quantities. Since they were first introduced in America only five years ago, first physicians and then the public have been offered such a confusing mass of advertising that a careful appraisal of their therapeutic value is warranted at this time.

Since the discovery of anaphylaxis and the recognition of its relationship to human allergy, many investigators have studied non-specific methods of preventing or controlling anaphylactic shock. In 1932, Hill and Martin[2] reviewed the results obtained by 165 such methods which were more or less effective in experimental animals; not one of these was applicable to the practical treatment of allergic disease in man.

Many other methods have since been proposed; of these the most successful are based on the concept of histamine as an intermediary between the antigen-antibody reaction and the manifestations of allergy and anaphylaxis. This theory, proposed by Dale and Laidlaw[3] in 1910, is supported by many researchers showing that histamine is released in anaphylactic shock and in allergies of the immediate urticarial type and gives rise to many of their chief manifestations. In certain aspects of anaphylaxis, such as the loss of coagulability of the blood in dogs, and in the delayed types of human allergy, such as tuberculin sensitization and contact dermatitis, histamine appears to play no part.

Within these limits, therapy directed at controlling the action of histamine offered the promise of a single form of treatment effective in

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many allergic diseases, without the need of determining the specific causative allergen. The earlier efforts in this direction, employing the enzyme histaminase, injections of histamine in attempts to induce tolerance, and histamine azo-protein (Hapamine) to produce antibodies to histamine, met with no significant success and have been abandoned.

In 1937, Staub and Bovet[4] reported investigations in experimental animals of the anti-anaphylactic and antihistaminic properties of a series of phenolic ethers synthesized by Fourneau. These properties were found to be shown to a significant degree by thymoxyethyl-diethylamine, designated as 929F, which may be considered the first synthetic antihistaminic but was too toxic for clinical use. The ethanolamine portion of its structure is utilized in the modern drugs Benadryl and Decapryn. Subsequently Staub[5] studied the antihistaminic properties of other synthetic compounds and showed that 1571F, an ethylene diamine derivative, was more potent than 929F, but still too toxic for clinical use. In 1942 Halpern[6] described a related compound, Antergan, which was 10 times as potent in animals and sufficiently safe for clinical use. This antihistaminic drug showed definite therapeutic effects in allergic rhinitis and urticaria, but was soon replaced by Neoantergan, another ethylenediamine compound which proved less toxic and more potent.

During the past war, while these studies were being made in France, American investigations led to the development of Benadryl, an ethanolamine derivative, and Pyribenzamine, an ethylenediamine compound related to Neoantergan. Both of these compounds had definite therapeutic effects in certain allergic diseases but were sufficiently toxic to stimulate further search for more potent and less toxic agents. During the past five years dozens of such compounds have been produced and screened by the drug industry and seventeen have been marketed, each with its own claims of potency and freedom from toxicity. The average physician is justifiably bewildered by this choice of essentially similar medications and may be comforted by the statement of the Council on Pharmacy that "the number of preparations on the market has served to provide confusion."[7]

The confusion is further increased by the application of both generic and proprietary names to each drug, and in many instances by the fact that the same drug is offered by two or more manufacturers under different proprietary names. For example, chlorcyclizine is marketed by Burroughs Wellcome as Perazil and by Abbott as Di-Paralene. In general,

the proprietary names are the most familiar and will be used in this discussion.

With the licensing of antihistaminic drugs for sale without prescription, many of the familiar drugs are being offered in reduced dosage under a variety of newly coined names. For example, pyranisamine 25 mg., familiar to physicians as Neoantergan, is offered to the public under thirty-two different names such as Kriptin, Anatamine, Macy's Antihistamine, Superhist, etc.

Chemistry: Chemically the twenty antihistaminic drugs more or less familiar to physicians, represent variations on a relatively few basic structures. The most commonly used structure is the ethylenediamine base (Fig. 1). In Pyrrolazote the nitrogen written at the left is included in a phenothiazine radical and that at the right is a pyrrolidine ring. In Antistine the 2nd carbon of the central chain is linked to 2 nitrogen atoms as part of an imidazoline ring, while in chlorcyclizine the 2 nitrogens form part of a piperazine ring rather than a simple chain.

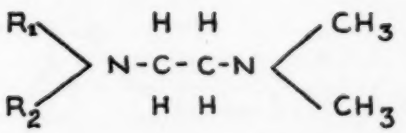

Fig. 1: Ethylene diamine structure. Antergan, Neoantergan, Pyribenzamine, Histadyl (Thenylene), chlorothen (Tagathen), Diatrin, Neohetramine and Thenfadil are represented by this formula with variations in the radicals R_1 and R_2.

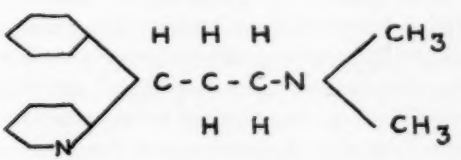

Fig. 2: Aminopropane structure. (Trimeton)

If the nitrogen at the left is replaced by carbon, the ethylenediamine structure is converted to aminopropane, but the antihistaminic activity is preserved, as in Trimeton and Chlor-Trimeton (Fig. 2).

If an oxygen atom or ether linkage is introduced at the same point, the ethanolamine series of antihistaminics, typified by Benadryl and Decapryn, is produced (Fig. 3).

The one chemically unique antihistaminic, Thephorin, has a complex ring structure based on pyridindene but is believed to break down in metabolism to a structure of the ethyldimethylamine type (Fig. 4).

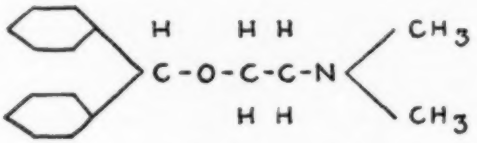

Fig. 3: Ethanolamine structure. (Benadryl)

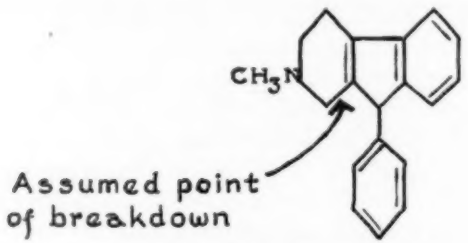

Fig. 4: Thephorin.

All of these are qualitatively similar in their pharmacologic actions, although differing quantitatively in antihistamine potency and toxicity.

Pharmacology: Pharmacologically, an antihistaminic drug has been defined by Bovet[8] as "a counterpoison having no specific activity of its own on the normal animal, its properties becoming apparent only when it can manifest a detoxifying power against the action of histamine." While the drugs marketed as antihistaminics represent the nearest approaches to this ideal found in screening hundreds of compounds, and all show definite antagonism to the actions of histamine, none can be said to be actually free of activity upon the normal animal.

The antagonism to histamine may be readily demonstrated by inhibition of the effects of histamine in causing contraction of smooth

muscle, capillary dilatation and wheal formation in the skin, hypotension and lachrymation. On the other hand, the stimulation of gastric secretion by histamine is not appreciably affected. The exact nature of the histamine antagonism has not been established but has been assumed to result from blocking the access of histamine to cell receptors.

Presumably through inhibiting the action of histamine as an intermediary, the antihistaminic drugs inhibit anaphylactic shock in guinea pigs, rabbits and dogs; also inhibit the Dale reaction in the isolated smooth muscle of the sensitized guinea pig. In adequate concentrations, these drugs inhibit the specific wheal reaction in the skin of allergic humans.

The other pharmacologic effects, considered as side effects, vary somewhat among the various drugs. Most of the group show a minor degree of atropine-like effect in antagonizing the actions of acetylcholine. The dry mouth of which some patients complain while taking the antihistaminics may be attributed to this action.

Practically all the antihistaminic drugs act as local anesthetics. Benadryl, Pyribenzamine and Neoantergan are said to be two or three times as active as procaine in this effect. Some authors have recommended the practical use of these drugs for this purpose and it is probable that their antipruritic effect as local applications may be due to action as anesthetics rather than antihistaminics. The relation of local anesthetic and antihistaminic effects is also of interest since procaine and its derivative diethylaminoethanol have been shown to inhibit allergic urticarial reactions. Local anesthetics may be expected to decrease the effects of histamine in the skin by blocking the axone reflexes which take part in the spread of the flare produced. The careful studies of Code[9] and his associates indicate that the inhibition of the histamine reaction in human skin by Benadryl, Pyribenzamine and Neoantergan is not dependent upon local anesthesia. These three drugs showed greater antihistaminic effects than concentrations of procaine equally effective as anesthetics, and their antihistaminic effect persisted after the local anesthetic effect wore off, while that of procaine did not. Furthermore, when many different antihistaminics were tested, it was found that those most effective as local anesthetics were often least active against histamine.

The actions of the antihistaminics on the central nervous system are among the most important side effects. In experimental animals, the nervous effect is usually excitement, but with ordinary doses in man,

sedation or depression is the usual effect. With the clinical use of the various drugs this may be apparent in 10 to 60 per cent of the patients, the incidence being highest with Benadryl and Decapryn.

Occasional individuals are excited rather than sedated by these drugs and in the case of Thephorin, excitement is the predominant nervous effect. With excessive doses of practically any of the drugs excitement and confusion of psychotic degree may result.

Choice of Drugs: The different antihistaminic drugs show considerable variations in efficacy and toxicity, but no one of them has a sufficiently greater ratio of potency to toxicity to be called the best. There are dozens of statistical reports of therapeutic and toxic effects of the various drugs but attempts to compare them are fraught with error because of variations in dosage used by various authors and differences in evaluation of results. An exact order of efficacy or toxicity cannot be established, but general classifications are helpful as a guide to physicians who can scarcely be expected to be familiar with all of the seventeen drugs that are available. In this grouping, I have borrowed freely from that given by Feinberg, Malkiel and Feinberg in their recent book "The Antihistamines."[10] Among the most potent drugs are Benadryl, Pyribenzamine, Neoantergan, Histadyl (Thenylene), Chlorathen and Decapryn. Of these Benadryl and Decapryn are the most sedative. A second group of drugs which are somewhat less potent but also less toxic includes Chlor-Trimeton and chlorcylizine (Perazil or Di-Paralene) which also have the advantage of longer duration of action. A third group of drugs less effective but valuable because of low toxicity includes Neohetramine, Antistine and Thephorin.

Such a classification does not accurately predict the reaction on each individual patient, but serves as a guide in selecting a drug for a particular purpose and in choosing a substitute if the one first tried proves ineffective or too toxic. For example, in mild hay fever one does well to choose a drug of relatively low toxicity, such as Perazil or Chlor-Trimeton, while for a patient confined to bed with intolerably itching urticaria, one of the most potent and most sedative drugs such as Benadryl or Decapryn is suitable. If a patient with rhinitis finds Pyribenzamine effective but too sedative, Neohetramine would be a more logical substitute than Benadryl, which is even more depressing.

Dosage Forms: All of the common antihistaminics are readily absorbed from the gastro-intestinal tract and are most commonly given

by mouth. They are marketed in pills or capsules containing one average adult dose which may be 4 to 100 mg. with different drugs. Details of dosage are different for each drug but in general the maximum dose is twice the average dose, repeated three to four times a day. Most of the drugs are also offered in liquid preparations for administration of fractional doses to children. The dosage of preparations offered for sale without a prescription is in general half the average dose offered to physicians.

The average duration of effect is about four hours, but the action of chlorcyclizine and Chlor-Trimeton is reported to last 8-12 hours.

In addition to the oral preparations, Benadryl and Histadyl are available in sterile solutions for intramuscular and intravenous use. These routes give prompter and often more powerful effects than oral administration.

For local application to itching eruptions most of the common antihistaminics are offered in ointments, creams and lotions. A few are offered in drops for ophthalmic or nasal use.

Uses: The primary purpose of the development of the antihistaminic drugs was the symptomatic relief of those allergic diseases in the pathogenesis of which histamine was known or believed to play a part, such as allergic rhinitis, asthma, urticaria, atopic dermatitis and serum sickness. Subsequently they have been tried empirically in many other diseases not known to be related to histamine. Such efficacy as they show is always in temporary symptomatic relief; in no disease are they curative. Even in those allergic disorders for which they have proved most useful, their efficacy is often surpassed by that of cortisone and ACTH.

For evaluation of their efficacy in various diseases, a host of statistics are available. When one attempts to consolidate various reports, however, it is apparent that the simple figures do not show the entire picture. In a single disease entity, mild and early cases many prove amenable to treatment while advanced cases are not. Some authors have used an "average dose" two or three times daily while others have prescribed two or three times as much four times a day. In evaluating results some have reported any significant degree of relief as a favorable result, while others have restricted this term to cases essentially free of symptoms. Therefore, we can best speak in general terms and use actual percentages of relief sparingly.

The most extensive clinical evaluation has been in allergic rhinitis.

Here the results obtained vary greatly with the severity and chronicity of the disease. In the acute stage of allergic rhinitis, either seasonal or non-seasonal, with sneezing, rhinorrhea and itching of the eyes and throat, satisfactory temporary relief may be obtained in 60-80 per cent of cases by use of the antihistaminics. On the other hand, the nasal obstruction due to engorgement of the mucosa, which is a prominent feature of long-standing rhinitis, is less susceptible to their action. Advanced rhinitis with polypoid changes in the membrane is only slightly affected. These differences are reflected in the statistics which usually show 60-75 per cent relief of seasonal hay fever and roughly 50 per cent for non-seasonal rhinitis.

In the case of hay fever, it means that patients with mild intermittent symptoms during the pollen season or with a short season caused by one of the tree pollens, may expect considerable relief from these drugs, while those who suffer continuously for 4-8 weeks during the grass or ragweed season will usually obtain only partial alleviation of symptoms. Since no other type of drugs except the recently introduced cortisone and ACTH offers as much symptomatic relief, the choice of treatment lies between the use of antihistaminics and the more elaborate and time-consuming method of prophylactic injections of pollen extract, started six or more weeks before the onset of the pollen season. Statistically the injection treatment is shown to be more effective but symptomatic treatment with antihistaminics has obvious advantages of simplicity and convenience. When the patient is first seen during the hay fever season, there is no opportunity for prophylactic injections and the antihistaminics should be used. The results obtained that season offer a basis for decision as to the choice of treatment in the following year. However, if pollen asthma occurs during the hay fever season, injection treatment is definitely indicated, since its occurrence is not appreciably prevented by the antihistaminics and it tends to become progressively more severe from year to year if other measures are not taken. On the other hand, a suitable course of pollen injections may be expected to relieve pollen asthma in 80 per cent of the cases.

This comparison of the effects of pollen injections and antihistaminics on hay fever does not mean that a choice must be made between them; the best results are obtained by combining both methods of treatment.

In non-seasonal allergic rhinitis it has been indicated that the anti-

histaminics are more effective for relief of acute symptoms than for persistent nasal congestion. Therefore, these drugs are most useful as a temporary measure and long-standing cases should be studied for determination of the causative factors. When the symptoms are due to sensitization to dust, animal danders or other inhalant allergens, much greater relief may be expected from allergic treatment than from continuous use of symptomatic drugs.

In bronchial asthma, the antihistaminics are considerably less effective than in allergic rhinitis. Many studies report 20-40 per cent of all asthmatics benefited by these drugs, but the patients relieved are almost invariably those with mild asthma usually more easily controlled by other oral medications such as ephedrine and aminophylline. In severe chronic asthma, when treatment is a real problem, the antihistaminics are generally useless. Certain proprietary combinations of antihistaminics with aminophyllin or ephedrine are moderately effective for the relief of mild asthma; but on the whole the antihistaminics offer no notable advance in the symptomatic relief of asthma.

Among the allergic dermatoses, urticaria is the most responsive to antihistaminic drugs. Most statistics indicate that 70-90 per cent of patients with acute urticaria are benefited by these medications. In some cases the "average dose" of the drug selected is effective, but often this must be doubled and repeated three or four times a day. In severe urticaria, intramuscular injections may be more effective than oral use. Relief of itching is often obtained although wheals may persist.

Chronic urticaria is somewhat less responsive than acute but the antihistaminics are still among the most valuable drugs for symptomatic relief. Continuous control may require large doses repeated three or four times daily. As in other chronic diseases, the effect of these drugs is only symptomatic and patients with urticaria persisting or recurring over a period of weeks should be carefully studied to determine the causative factors.

Angioedema or giant urticaria is less susceptible to these drugs but it is also relatively resistant to most other forms of treatment, so a trial of their efficacy is warranted. In acute attacks, large doses of antihistaminics by mouth or injected parenterally may be used concurrently with injections of epinephrine in oil. For prevention of recurrent attacks continuous use of one of the antihistaminics may be advised, but as in chronic urticaria, a diligent search for etiologic factors should be made.

The antihistaminics are of definite value in treatment of serum sickness and similar reactions to penicillin. Relatively large doses are required and intramuscular administration may be more effective. The effects are chiefly in the relief of itching and urticaria; arthralgia and fever are not appreciably affected. In very severe cases, the antihistaminics may prove ineffectual and ACTH or cortisone should be used.

In severe anaphylactic reactions resulting from the injection of heterologous antisera or other biologic products, the effect of the antihistaminics is too slow to be the main therapeutic effort. Epinephrine is more rapid and efficacious, but its action may be supplemented by parenteral injections of Benadryl or Histadyl.

The antihistaminic drugs have been widely used in atopic dermatitis, but estimates of favorable results have been reported by various authors as 0 to 75 per cent. This discrepancy is due to the fact that more than half of the patients treated have some relief of itching but there is no immediate change in the appearance of the skin lesions such as is produced by cortisone and ACTH. However, since itching is one of the most troublesome symptoms of atopic dermatitis and a considerable part of the objective change in the skin results from scratching and secondary infection, control of the itching constitutes an important part of treatment. For this purpose, the antihistaminics are among the most effective systemic medications. When the itching is severe, the drugs having a pronounced sedative effect such as Benadryl and Decapryn are most effective. In addition to oral preparations, many of the drugs are supplied in ointments, creams and lotions for local applications. Such preparations are reasonably effective in the control of itching, either through local anesthetic or antihistaminic actions.

Contact dermatitis, in contrast to atopic dermatitis, is a delayed form of allergic reaction in the pathogenesis of which histamine has not been shown to play a part. However, empirical trial of the antihistaminics, both as oral medications and topical applications, has been found to afford some relief of itching but not to alter the appearance or direction of the lesions. Indeed the antipruritic effect of these drugs is by no means limited to the allergic dermatoses. Itching due to such varied causes as chicken pox, jaundice and Hodgkin's disease may be alleviated to some degree by the local or general use of antihistaminics. Here again, these drugs may be exerting an anesthetic action on the nerve endings and one need not assume that histamine is being an-

tagonized. In pruritus ani and vulvae, moderate relief comparable to that afforded by local anesthetics of the procaine group may be attained.

Trials of antihistaminic drugs in cases of gastrointestinal allergy have given some favorable results but experience in this field is limited. In evaluating the results one must remember that many of these drugs have sedative and anti-cholinergic as well as specific antihistaminic effects.

In the type of headaches classed as histamine cephalalgia, the results are on the whole disappointing. Satisfactory control is rarely obtained with the antihistaminics. Such failures cast some doubt on the diagnosis but it may be recalled that not all known effects of histamine, such as that on the gastric secretion, are prevented by these drugs. Also in migraine attributed to food allergy, the results are generally disappointing.

As in contact dermatitis, the antihistaminic drugs have been applied empirically or illogically to other forms of hypersensitivity in which histamine has not been shown to play a part. For example, these drugs have been administered to patients with pulmonary tuberculosis in an attempt to eliminate the factor of tuberculin sensitization from the pathogenesis of the disease. The clinical results of such therapy are not convincing and most careful studies have shown that the readily observed manifestation of the sensitization. namely the cutaneous reaction to the tuberculin test, is not inhibited by the antihistaminics.

The results obtained in allergic reactions to drugs are variable as are the mechanisms of these reactions. In general, urticarial reactions in which histamine is presumably a factor, are benefited while other manifestations of drug sensitization such as drug fever, dermatitis medicamentosa and leukopenia, are not. Histamine-like reactions to injections of Diodrast are not prevented by prophylactic use of antihistaminics. Bronchospastic reactions to curare, believed to result from release of histamine, are benefited.[11]

In view of the similarity of symptoms of the common cold and allergic rhinitis, it is not surprising that the effects of antihistaminics on virus rhinitis were soon tested. In 1945 Troescher-Elam, Ancona and Kerr[12] reported the presence of a histamine-like substance in the nasal secretions of patients with common colds. This study has not been confirmed, but in 1949 Fox and Livingston,[13] without conclusive evidence, expressed the opinion that allergy to the cold virus played a prominent

part in the pathogenesis of the cold.

Actual use of Benadryl in the treatment of the common cold with apparently brilliant results was reported by Brewster in 1947 in the U.S. Navy Medical Bulletin.[14] This and four subsequent reports by the same author stressed the point that the use of Benadryl during the first few hours after the onset of a cold brought about recovery within twenty-four hours in a large proportion of colds. Murray[15] and also Gordon[16] published similar reports and a more carefully controlled study by Arminio and Sweet[17] indicated that the antihistaminics were effective in the prevention and cure of colds. These reports were analyzed by the Council on Pharmacy[18] and criticized on the grounds of the diagnostic criteria, failure to exclude allergic rhinitis adequately, lack of suitable control groups in most cases, and the methods of compiling statistics. The Council suggested that inoculation of volunteers with a potent strain of cold virus would offer the best basis for a controlled trial.

Such an experimental inoculation study was undertaken by Feller and associates[19] while other groups started carefully controlled observations on natural colds in large groups of individuals. Before the results were obtained, the matter became one of public controversy as well as scientific inquiry. The claims of Brewster were presented to the public in a sensational and uncritical article in the Reader's Digest[20] as the long-awaited preventative and cure of the common cold. At about the same time, the Federal Food and Drug Administration permitted the sale of certain antihistaminics without prescriptions and the manufacturers were quick to exploit their use for common colds in spectacular advertising, much of which claimed or implied the approval of not only the Reader's Digest but also the Navy Medical Department and the Food and Drug Administration. In March of 1950 the Federal Trade Commission entered complaints against five of the largest manufacturers of antihistaminic drugs for over-the-counter sales, charging misrepresentation of the efficacy of these compounds in the prevention and cure of the common cold. With millions of dollars of sales at stake and the public having been promised an effective cure of the common cold, the controversy aroused great interest in the press but was settled within a few months with the manufacturers agreeing to advertise that the antihistaminics relieve the symptoms of colds rather than being effective cures.

During the past six months many reports of carefully controlled studies have shown that the antihistaminics have little or no value in preventing or curing the common cold. Experimental inoculations of volunteers with cold virus by Feller and associates[19] showed that these drugs had no effect in prevention of colds. Shaw and Wightman[21] at Cornell, Cowan and Diehl[22] at the University of Minnesota, Hoagland[23] at West Point and a group of workers in the Navy[24] all presented careful reports of the treatment of large series of patients with colds with comparable groups receiving antihistaminic drugs and placebos as controls. In every case the results in the antihistamine-treated and control groups were essentially the same. It was a striking find that in every instance the patients given inert placebos reported considerable benefits. Cowan and Diehl reported that one student who returned to the university after graduation specifically to obtain some more of the medication was found to belong to the control group.

The consensus of medical evidence supports the opinion that the antihistaminic drugs are not effective in the prevention or cure of the common cold. The person who takes a pill after the first sneeze or sniffle cannot be sure that he is suffering from a cold infection rather than the effects of a chill, draft or minor allergy and so is not helpful as a part of a scientific experiment. Some of the early symptoms of a cold such as sneezing and rhinorrhea are in many cases relieved partially or completely by the antihistaminics, as they are by atropine, but the progress of the infection is not stopped. Patients with chronic allergic rhinitis and superimposed acute colds may enjoy greater benefit, both directly from relief of the allergic component and indirectly from the fact that the resistance of the mucosa to infection is greater when it is not coincidentally involved with an allergic reaction.

Aside from their use in the common cold, antihistaminic drugs have been found to have unforeseen uses in certain diseases unrelated to allergy. Dramamine, a derivative of Benadryl, attracted such attention as a remedy for motion sickness that its use as an antihistaminic has been neglected. Subsequent studies have shown that Benadryl itself is equally effective in the relief of motion sickness and that Neoantergan is also beneficial. Dramamine has also been used but with less definite results in Ménière's disease and in nausea and vomiting due to pregnancy and many other causes. Benadryl has been found beneficial in the relief of Parkinson's disease and several of the other antihistaminics have been

shown to have palliative effects comparable to other available drugs.

Isolated reports have described various antihistaminics as being of value in dysmenorrhea, irradiation sickness, ulcerative stomatitis, bee stings and snake bite. In most of these cases the evidence presented is scanty and confirmation lacking as yet.

Untoward Effects: As previously mentioned, no drug yet developed is purely antihistaminic in its activity; all show other pharmacologic actions which are undesirable side effects. The best known of these is the sedative effect produced in 10 to 60 per cent of patients by ordinary doses. This effect is most marked with drugs of the aminoethanol group such as Benadryl and Decapryn, less marked with Thephorin and Neohetramine. The undesirability of this action must be weighed against the severity of the symptoms for which the drug is given. Not infrequently the patient may consider the treatment worse than the disease. It is particularly important since many of the conditions for which antihistaminics are used are not disabling and the patient remains ambulatory and employed during treatment. Thus drowsiness may lead to serious errors of judgment in business or failure of performance in operating automobiles and other machines. On the other hand, in patients confined to bed with intolerable itching, mild sedation may be helpful.

With gross overdosage, the usual mental effect is confusion and excitement rather than somnolence. In severe cases this may result in an acute toxic psychosis with hallucinations and delusions. Several fatalities have been reported in children.

In idiopathic epilepsy and seizures due to focal lesions of the cerebral cortex, Benadryl and Pyribenzamine have been shown to increase the frequency of seizures.[25] In the absence of specific data on the other drugs of the group, it is apparent that all antihistaminics should be used with caution, if at all, in patients with convulsive seizures.

Since many of the antihistaminics have a mild atropine-like effect, some patients will complain of dryness of the mouth and throat. Gastrointestinal irritation, manifested by nausea, vomiting, diarrhea or abdominal cramps, is not uncommon when large doses are given between or before meals. In many cases, this may be avoided by administration after meals, in others a different drug of the group may be substituted.

Prolonged administration of large doses of antihistaminics of the ethylenediamine group has occasionally resulted in leukopenia or agranu-

*l*ocytosis. A half-dozen such cases have been reported, most of which have followed the use of Pyribenzamine. However, since this is one of the oldest and most widely used drugs of the group, it would appear that the predominance may be due simply to more extensive use. While the danger of this type of reaction does not appear to be great, prolonged use of full doses should be avoided if possible, and if the need persists, the blood should be examined periodically.

Drug rashes from the oral use of antihistaminics have been reported but are rare. On the other hand, contact dermatitis from local application of these drugs to the skin is relatively common if use is continued for more than one or two weeks. With most topical antihistaminic preparations an incidence of sensitization of 2 to 5 per cent may be expected.

Summary

The available antihistaminic drugs are all essentially similar in their action and side effects although varying both in potency and toxicity. No one drug may be said to be the best. These drugs are of value for symptomatic relief in allergic rhinitis, urticaria and serum sickness and for the control of itching. In no disease do they have a curative effect. In asthma, their efficacy is less than that of older drugs. In the treatment of the common colds they do not alter the course of the infection but may afford some symptomatic relief. The commoner side effects are drowsiness and nausea. Long continued use occasionally leads to leukopenia or agranulocytosis. Contact dermatitis not infrequently results from their topical use. On the whole, these drugs represent a definite contribution to therapy but there is still room for newer compounds with greater potency and less toxic effects. In most of the allergic diseases, their efficacy is surpassed by that of cortisone and ACTH.

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REPORT ON CONVALESCENT CARE

by the

COMMITTEE ON PUBLIC HEALTH RELATIONS*

THE NEW YORK ACADEMY OF MEDICINE

CONVALESCENT care has never been more than a minor phase of the provision which the City of New York makes for the medical care of the sick and injured who are its charges. Although nearly half the hospital beds in the city are in municipal institutions, the city has never built or operated a convalescent hospital.

A few efforts have been made to provide some kind of service for those who have passed the acute phase of illness, but are unable for any reason to resume their vocational activities. One approach was the establishment by the Department of Hospitals of a Convalescent Day Camp on Welfare Island in 1939, to meet the needs of those for whom no facilities were available. The camp was apparently successful to a degree, but its location was a drawback, and after the WPA workers who made up most of its staff were withdrawn, it was closed. The late Dr. S. S. Goldwater, as Commissioner of Hospitals, envisioned the construction of facilities on hospital roofs, but this idea was never carried out.

The Department of Hospitals has for many years authorized the care of city patients in private convalescent institutions under certain conditions. The amounts appropriated from the Charitable Institutions Budget of the city have varied from year to year, but until recently the trend has been downward in spite of the fact that the per diem rate paid has been gradually raised. More city charges were placed in convalescent institutions in 1949 than in 1948, but the slight increase was not sufficient to relieve the severe overcrowding in the municipal hospitals.

There are several reasons for the city's limited use of convalescent care, aside from advances in medical treatment which have shortened the duration of many illnesses and prevented complications in others. Many convalescent homes have so restricted their admissions that certain types of patients are excluded. At the same time the Department of Hospitals has had no clear-cut rules to indicate the types of cases eligible for reimbursement by the city; a set of rules and regulations was issued in 1933, but these are said to have been out of print for at least ten years. The suitability of patients for convalescent care has been determined according to the individual circumstances.

The present situation is also partly attributable to other factors which have been repeatedly brought out in the various studies and conferences sponsored by the Committee on Public Health Relations of The New York Academy of Medicine and other agencies during the past twenty-five years. These factors include: inadequate medical supervision in some of the institutions; the preoccupation of clinicians with the acute phase of illness and their consequent lack of interest in the recovery phase; the failure of hospitals to furnish sufficient information and directions for the care of the patients, the absence of a continuing liaison between convalescent institutions and hospitals, and the seasonal operation of some of the establishments.

In the election of November 1949, the voters approved a bond issue of $150,000,000 to be used for the improvement and ex-

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pansion of the facilities for hospital care in New York City. The Commissioner of Hospitals thus has an opportunity to launch a constructive program of convalescent care. He is persuaded that in the proper utilization of convalescent care lies an opportunity to relieve the overcrowding in city hospitals, as well as to provide needed care for patients. To guide him in developing the program, he has asked the Committee on Public Health Relations to present 1) standards of care and equipment in convalescent institutions; 2) determinations of the types of patients who would benefit from care in such institutions; 3) suggestions for rules and regulations to be exercised by the Department; and 4) recommendations as to the rates that should be paid by the City for the care to be provided in voluntary institutions.

The Committee has considered all these problems and has prepared the attached summary.

Classification of Convalescent Institutions

Recent departures in medical care, particularly the general adoption of the principle of early ambulation and the development of methods for active treatment during recovery, have thrust a new role on institutions that provide convalescent care. The Master Plan for Hospitals and Related Facilities for New York City defined convalescent care in terms of time as beginning "early after the acute phase of illness or injury," and continuing "until complete recovery or rehabilitation has been attained." This concept assumes that institutions for convalescence should be prepared to offer more medical service than has been expected of them in the past. It implies also that many more beds will be required than are available at present.

The Master Plan estimated that one bed per thousand of population should be available for convalescence and recommended that units for convalescent care should be established in general hospitals. The Plan recommended further that the number of convalescent beds in each hospital should be equivalent to about one-fourth of its general care beds and that no unit should have less than fifty beds. Emphasis was placed on the need for continuity of medical care and the need for research, both of which would be encouraged by the close association of the general hospital with facilities for convalescent care.

The Committee recognizes that the arrangements suggested in the Master Plan represent a goal which may not be reached for many years. Meanwhile, institutions located outside the urban areas afford the advantages of the country, which are of importance in expediting the recovery of some people sent to them mainly for upbuilding. The Department of Hospitals may profitably expand its use of the existing institutions. Although in the past most of them have operated independently, with inadequate channels of communication to hospitals and therefore no means of maintaining any continuity in medical care and no uniform standards, the recent formation of the Conference Group on Convalescent Care under the auspices of the United Hospital Fund has been a helpful influence. It serves as a vehicle for stimulating improvement of services by ascertaining the nature of community needs, suggesting adaptation of programs in line with the needs, and bringing into closer relationship the staffs of the convalescent institutions and the hospitals.

For the development of a program in the field of convalescence it seems desirable that either the State Department of Social Welfare or the Hospital Council of Greater New York, undertake the job of classifying the existing facilities. It appears that the time has come for a differentiation among the various types according to the services they offer. Accommodations should be available, first, for those who require rest after a period of illness; second, for those who need a certain amount of medical care plus rest, and third, for those who need active rehabilitation. Institutions for custodial care, as well as nursing homes for the chronically ill, are excluded from this discussion, since these patients do not come within the category of convalescents.*

* The State Department of Social Welfare has recently issued a report on these two types of establishments.

Rest Homes: The Committee is of the opinion that many of the existing convalescent homes which offer only rest in the country and good food are simply rest homes and should be so designated. The services they offer are primarily nonmedical and are appropriate for patients recovering from uncomplicated medical and surgical conditions, for patients who need a period of building up before a surgical operation, and for tired mothers and undernourished children. Such homes should not, however, be used as resorts for well children during the summer; vacations should be provided by other agencies.

General Convalescent Hospitals: The greatest need in the field of convalescent care is for a sufficient number of well organized, well equipped convalescent hospitals to furnish medical and nursing care to those who are recovering from severe illness or injuries. Municipal hospitals in New York City are so overcrowded that they are under constant pressure to release patients at the earliest possible time, yet it is difficult to do this unless proper care is continued elsewhere. Another impelling factor in early discharges is the conviction developed within the past two decades and reinforced by the experience with the wounded in World War II that hospital patients, particularly those who have undergone surgical operations, profit by an early return to physical activity. Although such patients may no longer need the services of the elaborately and expensively equipped hospital, most of them are still sick and they do need medical attention which they may or may not be able to secure in their own homes.

The majority of convalescent patients may be cared for in general convalescent hospitals. In the past convalescent homes restricted their admissions rigidly to exclude many categories of disease or infirmity, but the present trend is toward more flexible policies. St. Luke's in Greenwich, Connecticut, for example, admits every kind of patient except bedridden adults, those with infectious disease in the communicable stage and psychotic patients; however, emotionally disturbed persons are accepted. Cancer patients are also admitted, though if they do not improve, facilities for terminal care are sought for them.

For some types of patients, those who require specific regimens and equipment, specialized services are needed. This group comprises patients with conditions complicated by epilepsy, cerebral palsy and orthopedic defects, some stages of rheumatic fever and heart disease with severely restricted physical activity, and tuberculosis. There is a need in New York for facilities to give care to young children cured of tuberculous meningitis and miliary tuberculosis; although their lesions are noncontagious, convalescent institutions do not accept these children. The situation is particularly difficult in the case of children under 3 years of age.

Rehabilitation Centers: During the past ten years the boundary between conditions in which some degree of rehabilitation is possible and those that are seemingly irreversible has become less and less sharply defined. It is now recognized that almost every type of convalescent institution should have some elements of a rehabilitation program. For the severely disabled, however, institutions especially equipped and staffed are essential. Such centers can function most beneficially when they are associated with hospitals and should be located in close proximity to them.

Home Care: Experiments in home care of the chronically ill have already proved the feasibility of this arrangement, and the Department of Hospitals has for the past two years carried on a limited program of home care for patients with both acute and chronic diseases. It would appear that "hospital care in the home," operated with visiting nurses and a homemaker service, could be extended to cover convalescent patients of various types, reducing the cost of care to the city and releasing beds for those who need them most. Foster home care is desirable for children.

Relationship to Hospitals

The Committee endorses the view set forth in the Master Plan that convalescent care is a phase of the complete treatment required by a patient and that continuity of medical supervision is essential. Under a

well integrated plan, facilities for convalescent patients should be parts of general hospitals, on separate floors or in wings, with specific programs arranged for the convalescent phase of medical care. In view of the large current demand for semi-private accommodations under voluntary prepayment plans for hospital care and the consequent decline in the use of ward facilities in voluntary hospitals, it is possible that these hospitals may find it desirable to convert a part of their ward space into units for convalescents.

To make possible continuity of medical care with the facilities now available, definite agreements should be developed between convalescent hospitals and general hospitals. There are already several patterns of organization in operation, and these might provide a basis upon which similar arrangements could be made for the municipal hospitals.

Some convalescent hospitals actually operate as units of general hospitals; the only difference from the goal set up in the Master Plan is that geographically the convalescent units are located at a distance from the parent hospital. Integrated medical supervision is achieved through coordinated policies.

Besides assuring the continuation of medical supervision, a formal relationship between a convalescent hospital and a general hospital makes for a satisfactory transfer of records. This is one of the thorniest problems which confront the two kinds of hospitals in their mutual dealings. Convalescent hospitals constantly report that patients are sent to them without adequate information on their conditions, their previous treatment and the treatment recommended for them during convalescence. Under a definite arrangement of the type suggested, the transfer of records or abstracts thereof can be made as a matter of routine, and the convalescent institution may admit patients earlier in their convalescence and may broaden its conditions of admission if it has access to the general hospital in the event of relapse or the development of intercurrent illnesses.

The parent hospital profits by close affiliation in that it affords opportunity for physicians and nurses on the staff to study the problems of convalescence. There is seldom any difficulty about placing patients when there is an actively functioning liaison. Moreover, considerable economy may be achieved through joint purchasing arrangements, and similar advantages accrue from a close bond between the other departments of the convalescent home and hospital.

Several types of interrelationships have been developed. In the case of the Mary Harkness Home, which is maintained by the Presbyterian Hospital, and in that of St. Luke's in New York, medical coordination is achieved by appointment of the chiefs of the convalescent services on the medical boards of the hospitals concerned. In the case of the Neustadter Home and Mount Sinai Hospital, both the home and hospital retain their separate identities, but the governing boards are interlocking and the medical director of the convalescent unit is a member of the medical staff of the hospital. A third arrangement that has proved successful is that under which St. John's Convalescent Hospital, Newtonbrook, Ontario, functions. This hospital has working agreements with seven hospitals in Toronto which take turns in providing the medical supervision for the convalescent institution, but there are no corporate relationships.

It seems desirable that the responsibility for medical care in a convalescent unit should be assumed by the staff of the general hospital. If more than one hospital is allied with a convalescent institution, the staff of the largest hospital might take on the responsibility of medical supervision. This, however, should not deprive the referring physicians of the opportunity to follow up their patients placed in the convalescent hospital. Such a program as that described need not exclude referrals from hospitals which have no specific agreements or from individual physicians.

Criteria

The Committee on Public Health Relations in 1925 formulated tentative standards for convalescent care of medical, surgical, neurological and pediatric patients. The standards for children were revised twice,

the last revision being in 1948. A review of standards for the entire field of convalescence is desirable. In New York State this might be taken up by the State Department of Social Welfare in association with professional bodies.

The supervision of the medical care program in a convalescent hospital by the medical staff of a general hospital will in itself assure adequate professional standards. It is desirable, however, to have an over-all formulation of standards which will be of particular value to institutions not connected with a hospital.

With the accelerated interest in convalescence has come recognition of the value of teamwork in the efforts to restore the sick and injured to usefulness. The modern approach is to make available to the patient in the convalescent hospital or rehabilitation center the coordinated services of a team of workers. Standards for convalescent hospitals should therefore include specifications and qualifications for personnel competent to give the necessary medical, nursing, rehabilitation and ancillary services.

The existing convalescent institutions have provided for medical staffs in several ways. Some utilize local physicians, with administrative responsibility vested in a resident director; some have separate staffs, and some are served by physicians from allied hospitals. The social worker has an important role in the organization; she is the link between the institution and the referring agencies, as well as between the patient and his family. Every institution should have a trained dietitian; this service might be on a part-time basis.

Vocational rehabilitation, which has proved its worth in the reestablishment of confidence and in hastening the worker's return to his job, or if necessary, his training in a new occupation, calls for trained counselors. This can be done best in a hospital unit. In institutions that are functioning for the time being outside hospitals, arrangements with the Division of Vocational Rehabilitation in the State Department of Education might be effected. Complete retraining as carried out in rehabilitation centers of the type developed during and since the war requires the highest type of experts, including physicians trained in the field of rehabilitation, physical and occupational therapists, teachers, social workers and psychologists.

Admissions: In institutions that are constituent parts of hospitals admission is a matter merely of transfer. In the other type of institution, the rigid admission policies of the past are yielding to a modern trend toward flexibility regarding age, sex, race, religion and types of disease. Segregation of patients should be practiced on certain broad bases. Adults and children should be placed in separate units, but some leeway as to the borderline between age groups should be allowed, particularly in the placement of adolescents or young adults, many of whom may be expected to adjust well with older people. Arbitrary upper age limits might well be discarded; the criteria for admission should be the degree of disability and the prognosis for improvement. It has been found that valuable service can be rendered to elderly patients if the medical and psychological criteria are applied thoughtfully.

Patients with neurological and psychiatric disorders may require segregation if they show such marked deviations from the normal as to disturb other patients; those with respiratory ailments should be separated if they are an undue source of infection or if they disturb others by coughing. Patients with cardiac or orthopedic disorders who require special regimens are best cared for in special units, and those who require unusual diets may best be handled in a group.

Length of Stay: The length of time a patient will need convalescent care cannot be determined with precision prior to his admission. Many patients require a briefer period than was anticipated; others require more time. Reports to the United Hospital Fund for the eight-year period 1940-1947 showed an average stay of 18.9 days in homes that restricted their service to adults. As would be expected, the stay in specialized homes was longer. Adults suffering from cardiac conditions spent, on the average, 37.1 days in the convalescent home; for cardiac children the average was 175.8.

Adults with neurological disorders required 36.7 days; children with this type of illness spent 49 days in convalescent facilities. In institutions caring for children with orthopedic disabilities the average time spent was 120 days.

No limitation as to length of stay should be specified on admission. While periods of stay for city cases must be approximated because of requirements of fiscal authorities, decisions as to the actual length of stay should be vested in the attending physicians.

Responsibility for Selection of Patients: The physician who has carried the responsibility for the medical care of the patient, either as an inpatient or an outpatient, is the logical person to decide on the need for convalescent care and to prescribe the regimen to be followed during the recovery period. He needs, however, the assistance of a social worker who is conversant with the patient's home situation as well as with the social, economic and emotional difficulties that have a bearing on the prognosis. Planning should be begun considerably in advance of the date of the patient's discharge from the hospital.

Types of Patients: There are three broad categories of patients who may be expected to benefit from convalescent care. These groups parallel in general the several required types of institutions, namely, the rest home, the convalescent hospital, and the rehabilitation center.

First are the patients who need only rest and relief from home cares and responsibilities for a short time, including children whose homes are unsuitable. They require little medical supervision and only simple nursing care. In this category would be included patients recovering from uncomplicated illnesses and operations, mothers with their newborn infants, persons with nutritional problems of a simple variety, and possibly some who need rest and physical upbuilding prior to elective surgery or between stage operations. Little use has been made so far of convalescent homes for building up patients before operations, but this seems to be a valid field for their services.

The second category of patients who need institutional care after a hospital experience consists of those who require active medical supervision, special dietary care, surgical dressings, physical therapy and training in caring for themselves. In general, they may be expected to return to their previous state of health and take up their former activities.

The third group of patients who need convalescent care is made up of those who have undergone irreversible changes and must therefore have a complete re-education and reorientation. The demonstrations during the past few years of the possibilities of rehabilitation for persons formerly considered to be in a hopeless condition have radically altered the application of the word "incurable." It is no longer acceptable to consign these patients to custodial care without an attempt to restore them to some degree of activity.

Many patients who are being treated in outpatient clinics would benefit from a stay in a convalescent hospital. In this group are many for whom an acute illness may be averted by a period of rest under medical observation, others who may need building up before surgical intervention, and still others whose surroundings are inimical to their recovery even from an illness that is not completely disabling. It would be desirable to include these among the convalescents for whom the city approves payment.

It is evident that care must be taken to assure the proper assignment of both hospital and ambulatory patients to institutions suited to individual needs.

Application Forms: A need which is receiving attention from the Conference Group on Convalescent Care is the amplification and standardization of application forms used by convalescent institutions. The forms vary from one institution to another in the information requested; they do not call for sufficient social and financial data, and the multiplicity of them makes for confusion and dissatisfaction. The Conference Group is attempting to evolve a uniform blank which will overcome the current defects. The necessity for detailed blanks would be obviated if close relationships existed between the convalescent and the general hospitals.

Difficulties in Placing Certain Types of Patients

Although the beds in some of the existing convalescent institutions are not being fully utilized, certain types of patients are unacceptable. Among these are borderline cases of nervous and mental diseases; epileptics; some blind convalescents; boys with rheumatic heart disease who are over 9 years old; both boys and girls between 12 and 17 years of age who have cardiac disease; both adults and children with orthopedic handicaps, especially older girls in body casts; mothers together with their small children; young children with tuberculosis in the convalescent stage; and Negro patients generally.

Clearing House

Until the principle of specific agreements between convalescent hospitals and general hospitals is more widely adopted, there is need for a central clearing house in the convalescent field such as is being maintained by the United Hospital Fund through the Conference Group on Convalescent Care and through the Counseling Service. The latter collects information about existing services and expedites placement of patients.

Research

Much remains to be learned concerning the conditions that underlie the phenomena of convalescence. It has been pointed out that the term "convalescence" is applied to the period following such diverse illnesses as lobar pneumonia, typhoid fever, duodenal ulcer, and such varied surgical procedures as thyroidectomy, herniotomy, or appendectomy. The convalescent states of these patients differ considerably.

In a convalescent hospital opportunity is afforded to observe the phenomena of the subsidence of disease. Such studies may contribute to the appraisal of medical and surgical procedures.

Research should be an integral part of a convalescent care program. There is opportunity for observation over long periods of such conditions as degenerative heart disease and arteriosclerosis, as well as for study of the emotional and nutritional aspects of the recovery process. Research should be undertaken, however, only in institutions that have the facilities of hospitals at their command.

The Administration of the City's Financial Aid

The Committee is of the opinion that the income schedule used by the Department of Hospitals in its determinations of the eligibility of patients for hospital care may also be used in determining eligibility for convalescent care. In considering the financial status of the convalescing patient, however, it should be borne in mind that medical indigency may begin at the time of his discharge from a hospital. A person who has been able to finance his own hospital care may have reached the limits of his financial ability and may be unable to afford further private care. The Committee wishes to point out that this income schedule is in need of revision, particularly in the section "Amount Applicable to Medical Care," with a view to raising the threshold for approvals by the City. Moreover, it should be correlated with the rating and budget scale used by the Health Department in its program of arranging for care for the physically handicapped. It is difficult for the administrators of convalescent institutions to plan with two city agencies using different concepts of evaluating and determining financial eligibility.

It is also urged that the rate schedule be applied consistently; convalescent homes have reported contrary decisions in comparable cases from different hospitals as well as reversals. At the present time the patient must be sent directly from the hospital to the convalescent home; otherwise the City will not pay for him. It appears that at the time the approval slip, "Application for Acceptance as City Charge in Convalescent Homes" (SR 1938-10M-10341) is sent by the hospital to the convalescent home, the city investigator may assure the hospital that the case will be approved. The convalescent home admits the patient and a month or six weeks later, the Department of Hospitals may refuse to pay. Yet the patient could not have been admitted to the convalescent institution unless he were transferred direct from the hospital; the hos-

pital could not keep him until the Department of Hospitals completed its investigation. In other words, the present procedure is often frustrating to both the hospital and the convalescent institution.

There is complaint of delay in transmitting approvals to the convalescent hospitals; in some instances the approval arrives after the patient has been discharged. The decision to transfer a patient for institutional convalescence should be made as early in the acute illness as is practical, in order to prevent delay, and inconvenience to the hospitals, the convalescent institution and the patient. If an extension of the stay of the patient is desired, application for that privilege must often be made before the original approval is received. These delays in relation to both acceptance and rejection place the convalescent homes in a difficult position as to their finances and in making plans for the acceptance of free patients.

Although the per diem rate of payment for convalescent care of city charges has been increased from $1.40 in 1943 to the present rate of $3.05, this amount does not meet the cost of care. As nearly as can be estimated, the present cost is from $6 to $8 per patient day in institutions offering active medical care.

Recommendations

I. The Department of Hospitals should extend its use of convalescent care for "city charges," not only as a means of service to patients, but also as a means of relieving the present overcrowding in the municipal hospitals and of reducing the cost to the city for the care of the sick. In planning new municipal hospitals the inclusion of convalescent services would be desirable.

II. The Department's program of home care should be extended to as many of their convalescent patients as have suitable homes.

III. To assure the maintenance of continuity in medical supervision of patients transferred from the municipal hospitals, it is recommended that the Department of Hospitals develop with convalescent institutions arrangements patterned after those described in this report.

IV. With special reference to payment for convalescent care by the City, the Committee recommends that the present restrictive policies with regard to approval of transfers and to the length of stay be modified so as to eliminate inconveniences to patients, hospitals and convalescent institutions. The Committee also proposes the following points for incorporation in a new formulation of rules and regulations:

1. In addition to those who are at present accepted as city charges for convalescent care, the following categories should be made eligible:

   a. Medically indigent patients in voluntary hospitals who have not been approved as city charges because their diagnoses do not fall within the designation of "Emergency not transferable to a municipal hospital," and such others as have been treated free in the voluntary hospitals.

   b. Those who were not medically indigent for their hospitalization but have become so at the point of convalescence.

   c. Those who are being treated in outpatient clinics, but who may need institutional convalescent care as much as do hospitalized patients. This group may include some of those who require special care in preparation for surgical operations or to prevent breakdowns.

2. Many of the patients included in the category of "chronic cases" should be certified for convalescent care after they have suffered exacerbations of their respective conditions or other intercurrent illnesses.

3. In view of the modern emphasis on rehabilitation, certain categories of persons of advanced age should be admitted, since many of them can attain some measure of economic usefulness.

4. The prevailing high maintenance costs justify a substantial increase in the city's allowance from the present figure of $3.05 per patient per day.

V. An important need is the classification of existing convalescent facilities into groups according to the type of service offered. The following categories are suggested: Convalescent hospitals, general and special; rehabilitation centers, and rest homes.

VI. In view of the diversity of practices in convalescent institutions, the Committee recommends that the State Department of

Social Welfare undertake, with the coöperation of medical bodies and lay organizations concerned with specific diseases, the tasks of classifying convalescent institutions and formulating standards for the several grades. For New York City the work of classification might possibly be delegated to the Hospital Council of Greater New York.

VII. The Committee recommends that in the preparation of standards, the following basic principles be borne in mind:

1. Convalescent institutions not associated with general hospitals should provide for a larger proportion of bed patients than have previously been accommodated.

2. The modern concept of the type of convalescent care to be provided in a general hospital justifies the allotment to this purpose of approximately one-fourth of the bed capacity of the hospital.

3. The medical, psychiatric, nursing, and dietetic, as well as the ancillary services of convalescent facilities should be organized to bring about a coordinated approach to the treatment of the patients.

4. The criterion for admission should be the likelihood of the patient's improvement, physically, psychologically, economically and socially.

5. Adults and children should not be placed together, but arbitrary rules as to age limits should be avoided.

6. Specialized services should be made available for certain groups of patients, but general convalescent hospitals should be equipped to handle patients recovering from a wide variety of ailments.

VIII. The Committee recommends that, since the "Regulations Governing Acceptance of Convalescent Cases as Public Charges" as issued in 1933 have become in many respects inapplicable, a new set of regulations be prepared, incorporating the principles set out in this report.

IX. All three types of institutions in the field of convalescence should be licensed by the State.

X. It is recommended that the United Hospital Fund's support of the Counseling Service and of the Conference Group on Convalescent Care be continued. Pending closer association of convalescent and general hospitals, such a clearing house as that provided by the Counseling Service fills a definite need.

XI. To provide a clearer picture of the prevalence of disability in this community, the Hospital Morbidity Reporting System recently initiated by the Departments of Hospitals and Health should eventually be extended to include records of convalescent patients.

XII. As a contribution toward the wider utilization of convalescent care and rehabilitation, the Committee recommends that efforts be made to bring about changes in the Workmen's Compensation Law, as well as in hospital and medical insurance plans which would make possible payment for convalescent care as a part of complete medical treatment.

XIII. Plans should be laid to take advantage of the provisions of a pending amendment to the Federal Vocational Rehabilitation Act, S. 4051, the Douglas-Lehman Bill, passed by the Senate and awaiting action by the House of Representatives, which, if enacted, will make available to appropriate institutions federal funds to finance rehabilitation and vocational training.

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Sippe, G. R. Nutritional macrocytic anaemia [in Mauritius]. London, Published on behalf of the Government of Mauritius by the Crown Agents for the Colonies, 1947, 76 p.

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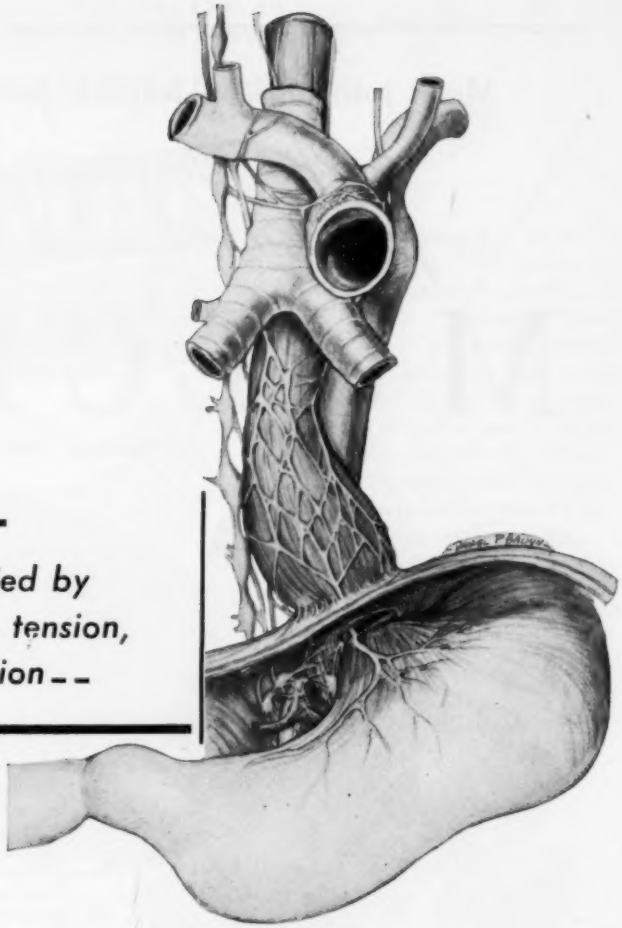

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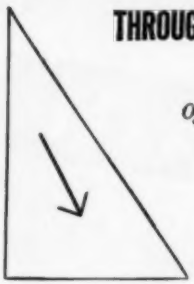

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*Kirwin, T. J., Lowsley, O. S., and Manning, J.: Effects of Pyridium in certain urogenital infections, *Am. J. Surg.* **62**: 330-335, December 1943.

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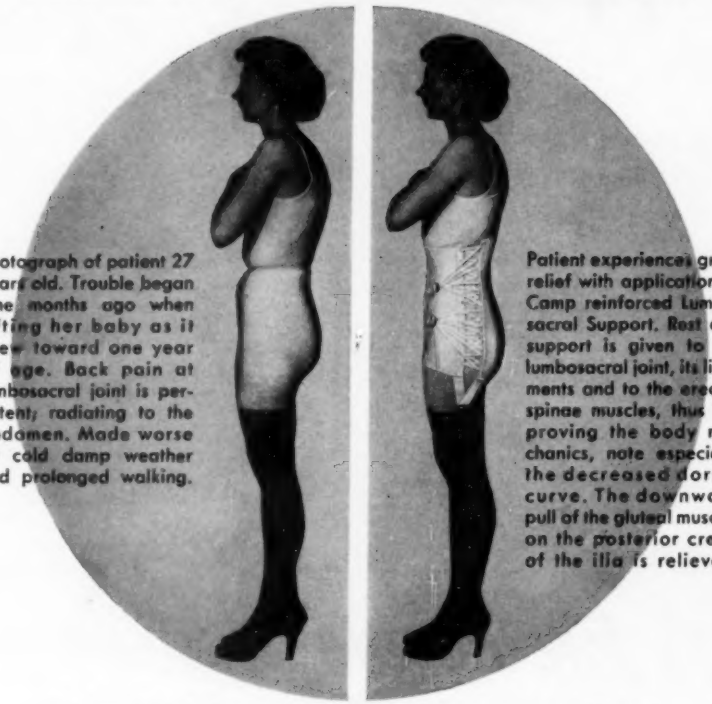

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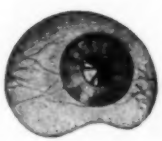

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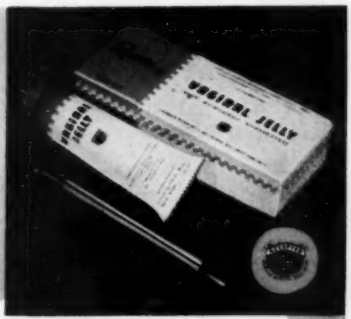

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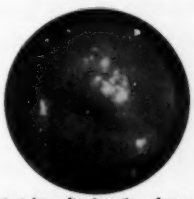

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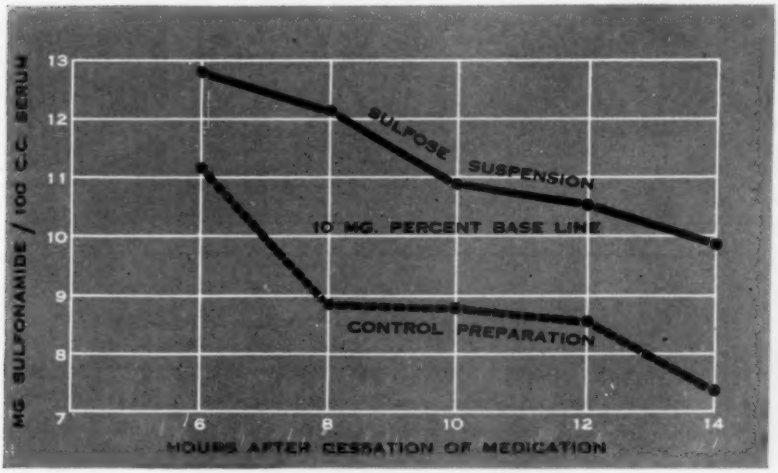

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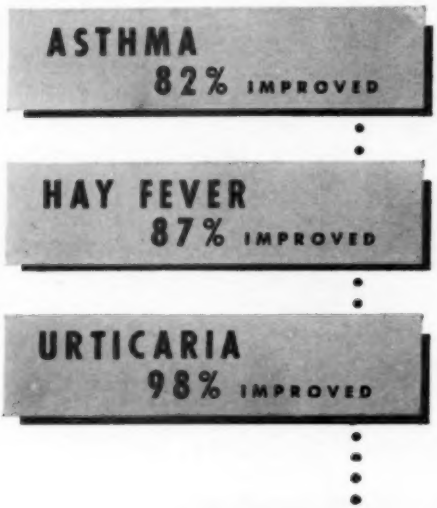

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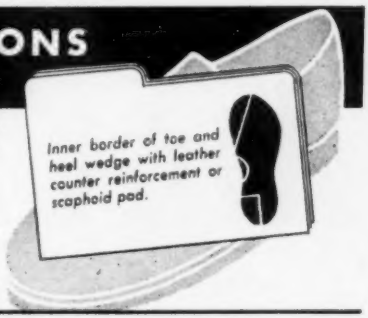

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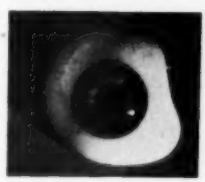

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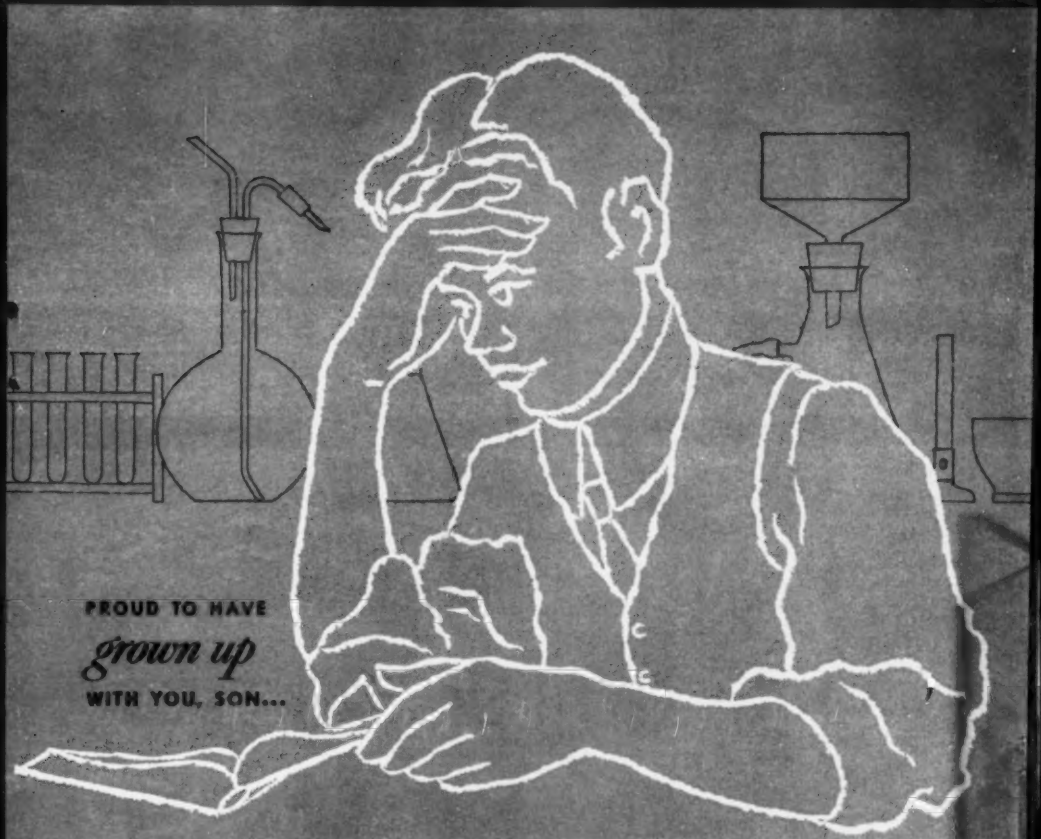

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Editorial: J.A.M.A. *135*:576, Nov. 1, 1947.

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Griggs, D. E., and Johns, V. J.: California Med. *69*:133, Aug. 1948.

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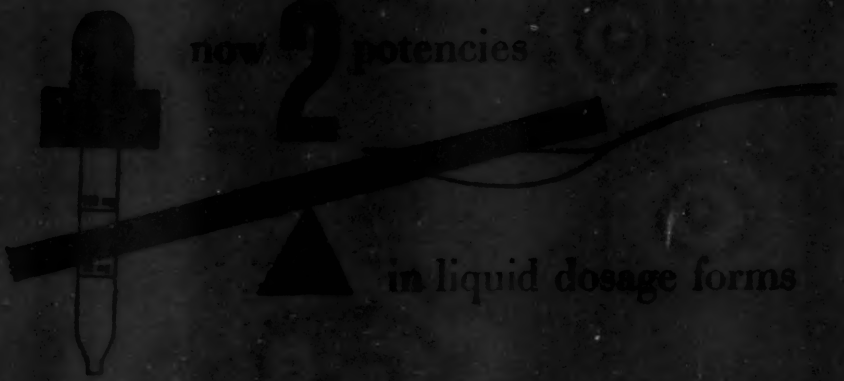

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